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"Regulation of the Use of Post-Operative Analgesia in Research Animals"

An Interactive Qualifying Project Report

Submitted to the Faculty

of the

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by

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Abstract

Regulations of post-operative procedures for laboratory canines are evaluated through the products of experiments, research articles. Information is acquired from *Anesthesia and Analgesia*, a medical journal, and the *American Journal for Veterinary Research*, a veterinary journal. Recent articles including procedures involving the thorax, abdomen, hips, or stifles are part of this study. Authors of research articles as well as local IACUC members are surveyed. The effectiveness of the system of regulation is examined and measures to strengthen it are suggested.

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1. Introduction

1.1 Background

The use of animal models for research purposes has been an invaluable and widely used tool for decades. In this age of rapid technological advances, the use of animals, such as canines, in the laboratory setting hastens the advance of life-saving and life-enhancing procedures, products, and techniques for use in humans as well as other animals. Often, advances requiring the use of these canines seem impossible to replace through any other avenue of research experimentation.

Although they are only one component of a large scientific process that supports technological advancement, canine research animals are still viewed as living creatures by a concerned public. Just like every other animal, laboratory animals need to be treated with proper care and spared as much discomfort and distress as possible. Many groups and organizations have been formed to ensure that these animals' welfare is properly defended. As Senator Bob Dole stated in his address to Congress in 1985, "We owe much to laboratory animals and that debt can best be repaid by good treatment and keeping painful experiments to a minimum."(Allen, 1999).

Animal welfare has been an issue in the minds of society and lawmakers for almost a century. The first animal welfare legislation in the United States was the "28-hour Law" of 1906(www.saplonline.org). This protected the welfare of livestock shipped by rail. Since that time, well over fifteen laws have been enacted regulating animal welfare. The most recent was the "Chimpanzee Health Improvement, Maintenance, and Protection Act," a bill that established a national sanctuary system for chimpanzees no longer used in biomedical research (www.saplonline.org). Many of these laws are passed

due to the support of various animal rights groups such as The Society for Animal Protective Legislation(SALP). Organizations like SALP and PAWS, the Progressive Animal Welfare Society, strive to educate the masses on the importance of animal welfare and the need for further legislation. In turn, it is the public's awareness and concern for animals that will continue to push the government to pass new laws that will benefit the well being of all animals, from household pets to livestock to wildlife to laboratory animals.

The greatest advancement in ensuring the proper care and treatment of laboratory animals came in 1966 with Congress's passing of the Animal Welfare Act. This act gives the United States Department of Agriculture (USDA) the authority to ensure the welfare of all animals used in regulated activities. This law lead to more expansive provisions including the "Improved Standards for Laboratory Animals Act" passed in 1995. This act refined humane care of animals and prompted the establishment of many of the agencies that regulate laboratory animal care today.

Current Regulatory System

In most parts of the developed world, legislation is in place to ensure humane treatment of laboratory animals (http://www.sciam.com/0297issue/0297trends.html). Currently in the United States there is a structure of regulatory oversight that has been put in place to ensure that an experimental procedure is efficient, non-repetitive, refined and humane. At the top of this chain of regulation, which is graphically illustrated in Figure 1, is the United States Government. The government controls are under the auspices of two important agencies that deal with the care of research animals, the United States

Department of Agriculture (USDA), and the National Institutes of Health (NIH). Both of these groups have put forth their own guidelines concerning the care of animals and the direction of Institutional Animal Care and Use Committees (IACUC). The USDA administers the Animal Welfare Act, which mandates that IACUCs assess each proposed protocol. They mandate that,

> "All animal activity proposals involving surgery must provide specific details of pre- through post-procedural care and relief of pain and distress... the attending veterinarian retains the authority to change post-operative care as necessary to ensure the comfort of the animal. The withholding of pain and/or distress relieving care must be scientifically justified in writing and approved by the IACUC. The appropriate use of drugs to relieve pain and/or distress must be specified in the animal activity proposal to avoid possible delays due to investigator concerns that a treatment regimen may interfere with the study. Furthermore, the specified drugs for relief of pain and/or distress must be readily available for use as described in the proposal." Animal Welfare Act, Section 13 and 9 CFR, Part 2, Sections 2.31, 2.32, 2.33, 2.40 and 9 CFR, Part 3, Section 3.110 (www.nal.usda.gov/awic/legislat/awa.htm).

The NIH oversees the Public Health Services (PHS), which has a set of guidelines very similar to the AWA, the Policy of Humane Care and Use of Laboratory Animals. In addition to the USDA and the NIH there is the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC). AAALAC is a voluntary program through which institutions can gain approval for their studies and laboratories provided the institution follows proper guidelines and policies (www.aaalac.org/html/about.html).

The IACUC, whose structure and functions are dictated by these agencies, controls the actions and proceedings of the individual research done at a certain facility. The IACUC regulates many aspects of the research process including the actions of their own members. For example, the method by which the committee reviews projects for approval and ensures studies are following proper protocols after approval are all controlled by the IACUC. This committee also supervises the overseeing veterinarian for each specific research project. The overseeing veterinarian is the on-site regulator, put in place to ensure the proper treatment of the animals. The IACUC also has responsibility for the personnel that work in the laboratory on the research project. Most importantly, by reviewing the protocol and total experiment proposal, the IACUC directly regulates the actions of the primary investigator, the researcher (Allen, 1999).

In addition to the IACUC, there are two other groups that aid in the regulation of proposed studies, funding agencies and journals. Before a project can get underway there must be adequate funding. In the academic setting, funding is not as readily available as it is in the corporate arena. Researchers who are not privately funded must seek external funding. There are many agencies, both government and private, that provide researchers with grant money for their work. In order to receive any grant money, the granting agency requires proof of IACUC approval. This is most commonly done by filling out a section on IACUC Protocol Form (Appendix A) requesting that written and signed approval for a study be sent to a specific granting agency. This insures that no study can receive funding without first receiving IACUC approval.

Another assurance that all studies have IACUC approval is put into effect by the scientific journals. The goal of many studies is to have the research published. Journals

require all articles to make some mention of the institution's approval as well as guidelines and policies followed. This is not a foolproof method however as the journal takes the word of the author(s) as to whether they have approval or not.

Figure 1: Current Path for the Regulation of the Care of Laboratory Animals

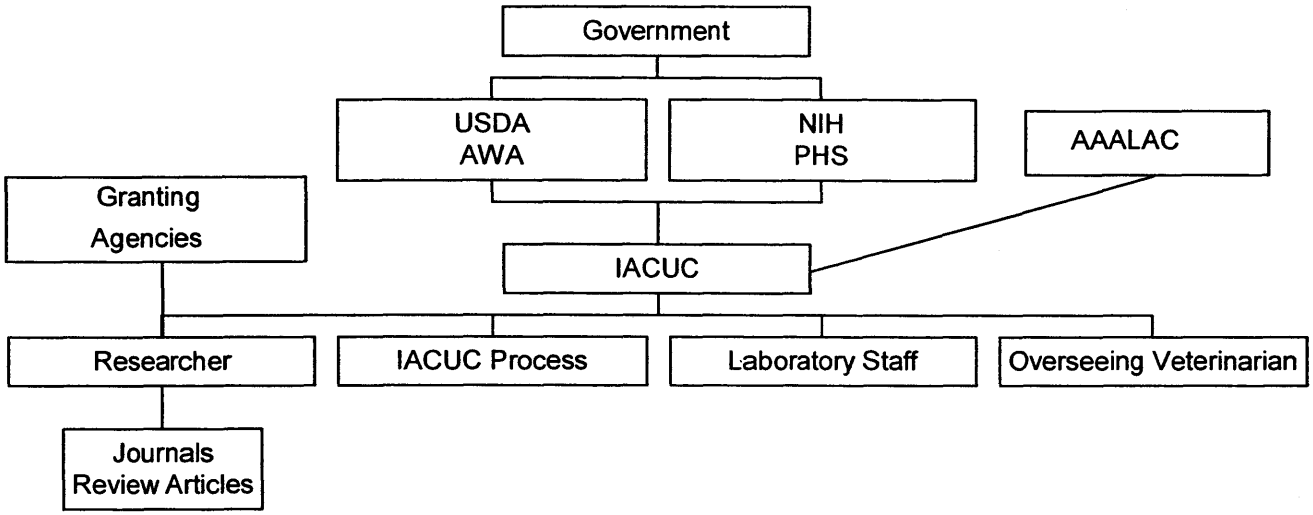

Figure I: Current Path for the Regulation of the Care of Laboratory Animals.

The government is divided into two subsections, the United States Department of Agriculture (USDA) and the National Institute of Health (NIH). The USDA is the agency responsible for the initiation of the Animal Welfare Act (AWA). The NIH controls the Public Health Services (PHS). The Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) is a voluntary program that certifies institutions demonstrating proper care and use of laboratory animals.

These three organizations and their policies control guidelines set forth for each individual Institutional Animal Care and Use Committee (IACUC). In turn, each IACUC also sets specifications for its own regulation process. All of the aforementioned entities affect the veterinarian overseeing the specific research project, the primary investigator (researcher) conducting study, as well as the laboratory staff.

Additionally, the researcher is regulated by any agencies providing funds for independent research in the form of grants. Written proof of IACUC approval is required before any funds are allocated.

The next form of regulation occurs when the completed study is submitted to a scientific journal for publication. The journal reviews the article, ensuring it states all necessary guidelines were followed and IACUC approval was obtained.

Flaws in the Current System

These precautions, combined with the additional legislation and guidelines in place, seem sufficient and reasonable to assure the well being of research animals. Regrettably, a large gap remains. There are insufficient guidelines as to what constitutes pain, or painful procedures, and appropriate treatment. There is a general lack of knowledge concerning the recognition and management of pain. (See Appendix B: The Problem with Assessing Pain.) Post-operative pain relief may be either inadequate or subject to over-administration. Also, as journal publication numbers continue to increase, oversight may decrease under pressure from technological and scientific advances. There is potential for pain management and assessment to become a minor or non-existent point in published accounts of research.

1.2 Purpose

The current study was undertaken to examine factors that may enable greater understanding of aspects and contributory factors relating to adequacy of pain management in laboratory animals. The findings of this study may also be used to pinpoint areas where further investigation would facilitate critical understanding to those seeking to enhance this system.

1.3 Study Design

If, as described above, a very detailed structure regulating care of laboratory animals exists, intact and functional, its success should be evident in resultant published research articles. Therefore, objective information such as the type of analgesics used, dosage and method of their administration, procedure for pain assessment, and frequency of such assessments should be disclosed in the product of research, articles written for scientific journals. At this level, the mechanism for and extent of control should be evident.

Journals

Articles from two monthly medical journals provided reports of post-operative procedure and analgesic use for this study. Very broadly speaking, the detail and quantity of such material should indirectly reflect views of the medical community. The properties of these reports should indicate expectations of publishers and, more importantly, members of the medical community who have written for, subscribed to, read, or referenced these journals. Publishers strive to ensure reader satisfaction; so consequently, article content will be a reflection of interests and priorities of the medical community. The quality of reports in articles, in terms of detailed disclosure of the aforementioned information, should yield rough indications of its relative importance.

To ensure more accurate conclusions, only recent articles involving painful experimental procedures were included in this study. Surgical procedures involving the abdominal or thoracic cavity, hip, or stifle, are universally perceived as painful. Thus,

reports of post-operative procedures following such procedures, from which canine models were allowed to recover, eliminate any question of analgesia necessity.

The two monthly medical journals used in this study differed significantly. One journal dealt with human medicine while the other, veterinary medicine. This distinction was conducive to further study conclusions, enabling investigation of relevant differences between procedures and information reported in each part of the medical field. Perhaps different portions of the scientific community, such as the medical or the veterinary components, deal with the subject of pain in animals in very different ways. A comparison between the two types of journals might help determine the role each type of scientific community assumes in reporting animal care and pain management.

Author Surveys

Published articles, though informative, contain data filtered by reviewers, intended for the public. For comparison, additional information was requested from an author of each article via survey. This questionnaire roughly quantified the level of experience reflected in the response but dealt primarily with the firsthand opinions and perceptions of individual researchers. Concern for canine models after painful procedures was questioned indirectly. Subjective views of policy effectiveness and enforcement, data accuracy, and the significance and effort assigned to humane measures were obtained. Most importantly, this survey presented an ideal method by which the existence and adequacy of any unpublished measures could be verified.

IACUC Surveys

The opinions and attitudes of IACUC members were also examined, due to the heavy regulation responsibility for animal research that has been designated to IACUC

members. These members deal closely with current policies and guidelines. They are most familiar with the present state of the regulatory system and should be most aware of any problems or weaknesses in its structure.

Logically, an IACUC questionnaire was created and distributed as a source of data. The first section of the questionnaire was used to define the subject in terms of demographical information. The second assessed attitudes toward general use of post-operative analgesia, and the final one examined perceptions of the manner in which post-operative analgesia is reported in medical journals.

The ultimate objective of this study as a whole is to gauge where the elaborate system of regulation weakens and why. It is to see what is reported, through the research articles, see what the reality is, via research author surveys, and to examine the views and standards of society that make it so by examining the feedback from the IACUC surveys. Resultant analysis of the system of regulation of pain management in the laboratory setting would lead us to propose improvements, to bring about an even more unfailing, refined, humane result.

2. Materials and Methods

2.1 Article Reviews

Only articles published in 1999 and 2000 were reviewed in this study. A procedure involving abdominal, thoracic, hip or stifle surgery on surviving laboratory canines was also necessary for article inclusion. Specifically, the type of surgery performed; the type of post-operative analgesic used; as well as the dosage, method of administration, frequency, and duration of analgesia were noted and recorded.

2.2 Research Author Surveys

Sixteen of the twenty-two relevant articles did not provide any information in regard to the use of post-operative analgesia. The authors were contacted and more information was requested via thirteen-question survey. Authors contacted were questioned regarding their perception of the current system as well as their thoughts regarding an ideal level of post-operative analgesia regulation. (See Fig I.)

Usually, article text named an author to whom correspondence should be directed. Therefore, it was appropriate to send out only one survey per article, though most publications listed at least three authors.

2.3 Article Publication

In order to examine the influence of editors and reviewers on the reports and practices of authors, a peer review checklist was requested from both journals. The resultant information is located in Appendices C and D.

2.4 IACUC Surveys

The questionnaire was distributed to forty members of various Institutional Animal Care and Use Committees (IACUC). The IACUCs surveyed included groups

from two academic settings, Tufts University and Worcester Polytechnic Institute. The first is a large institution with extensive research facilities, including a school of veterinary medicine and many animals available as research subjects. This AAALAC-accredited institution receives federal funding from agencies such as the USDA and NIH. The second institution is a small, private university with very limited research facilities for investigations involving animals. The only small vertebrates used in their facilities are rats, mice, and rabbits. Both institutions strive for advancements in basic science research.

The questionnaire was also distributed to two biotechnology corporations of similar size. Both companies are profit-oriented and only engage in research that may lead to a product or a patent. The management of these companies, in contrast to the universities, exhibits much more control over the research processes as well as the personnel and any public relations.

The questionnaire sent to the universities and corporations dealt with subjective assessments of the system. Information was requested regarding what the person felt was adequate in terms of monitoring and medicating the pain of post-operative animals. Also, the subjective impression of current laws and their effectiveness was assessed.

3. Results

3.1 Article Reviews

Many areas of data collection were involved in this study. Articles from two journals were reviewed and specific information regarding the use of post-operative analgesia was extracted. (See Tables I, II, III.)

Of the twenty-two articles identified as meeting the inclusion criteria for this study, nineteen came from the *American Journal of Veterinary Research* and only four from *Anesthesia and Analgesia.* (Table III.) When these were divided into surgical categories, there were a total of nine articles including abdominal surgery, three hip, three knee, and seven thorax.

Use of post-operative analgesia was reported for none of those involving the knee and twenty-two, sixty-seven, and twenty-nine percent of those involving abdominal, hip, and thoracic surgery, respectively. (Table IIIC.) These numbers for all studies are identical to those for *AJVR* articles, because *AJVR* was the source of an overwhelming majority of the articles.

Journal (Year)	Volume, Page	Procedure	Post-Op Meds	Dosage/Method	Frequency	Duration
AJVR (1999)	60.2, 181	Insertion hepatic vein catheter. Entry through abdomen.	*	*	*	*
	60.3, 281	Cylinders placed in thorax.	*	*	*	*
	60.5, 397	Midline celiotomy. Electrode implants. (abdomen)	Cephapirin sodium	20mg/kg, IV	Q8	24 hours
	60.5, 636	Bone marrow collection from illeum.(abdomen)	*	*	*	*
	60.8, 922	Carinolateral approach to coxafemoral joint and remodeling of femur.(hip)	Butorphanol	0.2mg/kg, IM	Q4 - Q6	24-36 hours
	60.8, 1011	Ventral midline abdominal incision. Ligation of bile ducts.	*	*	*	*
	60.9, 1164	Surgical repair of cranial cruciate ligament. (knee)	*	*	*	*
	60.11, 1337	Unilateral total hip replacement.	Butorphanol	0.1mg/kg, IM	"Immediately as needed"	
	60.11, 1383	Midline laparotomy. Ventral cystotomy. (abdomen)	*	*	*	*
	60.12, 1571	Unilateral TPO (hip).	*	*	*	*
	61.2, 121	Ovariohysterectomy (abdomen)	*	*	*	*
AJVR (2000)	61.5, 484	Osteotomy of pubis, ischium, and illeum. (abdomen)	Acetominophen	5mg/kg PO	Q8	3 days
			Codine	1mg.kg PO	Q8	3 days
	61.5, 530	Lateral approach of the stifle. (knee)	*	*	*	*
	61.8, 960	Placement of ECG electrodes in thorax.	Buprenophine	5ug/kg IM	"As needed."	
	61.10, 1273	Placement of urinary catheter. (abdomen)	*	*	*	*
	61.11, 1415	Ventral midline laparotomy. Removal of 1g of rectum. (abdomen)	*	*	*	*
	61.12, 1534	Placement of femoral artery catheter and renal artery clip. (thorax)	*	*	*	*
	61.12, 1593	Placement of aorticarch and right atrium catheters. (thorax)	*	*	*	*

Table I: Data collected from *American Journal of Veterinary Research.* All information published in 1999 or 2000. All articles based on surgical procedure involving canine thorax, abdomen, hip, or knee. Table I illustrates the reporting of specific information regarding post-operative medications. A "*" indicates information absent from article.

Journal (Year)	Volume, Page	Procedure	Post-Op Meds	Dosage/Method	Frequency	Duration
A&A (1999)						
	89, 409	Lateral radiocarpal inflammation. (knee)	*	*	*	*
	89, 1393	Left thoracotomy. (thorax)	*	*	*	*
A&A (2000)						
	91, 787	Left thoracotomy. (thorax)	pitramide	15mg/kg IM	Q2	3 days
	91, 1333	Left thoracotomy. (thorax)	*	*	*	*

Table II: Data collected from *Anesthesia and Analgesia.* All information published in 1999 or 2000. All articles based on surgical procedure involving canine thorax, abdomen, hip, or knee. Table I illustrates the reporting of specific information regarding post-operative medications. A "*" indicates information absent from article.

A.

American Journal of Veterinary Research Articles
1999-2000

Area of Surgery	Total Number of Articles	Reported Post-Op Analgesia
Abdomen	9	2
Hip	3	2
Knee	2	0
Thorax	4	1
Total	18	5

Area of Surgery	Total Number of Articles	% Reporting Post-Op Analgesia
Abdomen	9	22
Hip	3	67
Knee	2	0
Thorax	4	25

B.

Anesthesia and Analgesia Articles
1999-2000

Area of Surgery	Total Number of Articles	Reported Post-Op Analgesia
Abdomen	0	0
Hip	0	0
Knee	1	0
Thorax	3	1
Total	4	1

C.

Combined Statistics (*AJVR* and *A&A)*

Area of Surgery	Total Number of Articles	Reported Post-Op Analgesia
Abdomen	9	2
Hip	3	2
Knee	3	0
Thorax	7	2
Total	22	6

Area of Surgery	Total Number of Articles	% Reporting Post-Op Analgesia
Abdomen	9	22
Hip	3	67
Knee	3	0
Thorax	7	29

Table III: Summary of data from Table I and Table II.

3.2 Research Author Surveys

Twenty-two surveys (Fig II) were sent to research article authors, and eleven contacted researchers replied. (See survey results, Table IV.) Therefore, the thirteen-question survey generated exactly 50% of the optimum resultant information. Six researchers indicated interest in reading this finished project; three declined. The remaining two had no response.

Portions of this questionnaire met varied responses rather than simply circled answers. Original, informative feedback was limited; the majority was unfortunately vague. Three authors presented question marks without additional comment. A couple questions were simply unanswered.

Researcher *b,* an AJVR author, took the time to return a note and blank survey. Her experience did not encompass the portion of research relevant to these questions.

Confusion and omission were more prevalent on certain questions. Researcher *a* omitted only number eleven, for which *e* and *k* wrote question marks and *c* and *d*, comments. Response from *c*: "A good question, as it has two answers. Survival is usually reported, [and] use of analgesia is less [frequently reported]." "N/A, publish if relevant," was written in by *d* for number eleven. Regrettably, author *e* similarly questioned numbers nine and ten.

Displaying initiative, *d* also selected both B and C in response to ten. This person indicated B was currently correct, though C had been accurate in the past.
The only other multiple responses were to question thirteen; author *f* circled A, B, and C without further comment. Also for thirteen, *i* answered, "Ethics committees based on

internationally accepted procedure." Researcher *j* answered with question marks on four and five, as well as thirteen, and wrote, "depends" near question eight.

Overall, this was an experienced group of researchers. (See Table V.) Eighty percent of the group had more than eleven years experience, half of those with more than sixteen.

Ninety percent believed the treatment of pain to be as important for canine models as any other dogs, including pets. Eighty percent considered any possible administration of post-operative analgesia important. A majority, sixty percent, favored a combination of objective and subjective pain assessment. Close to one-third of this group favored subjective measures alone.

Sixty percent indicated that checking a surgically recovering canine for pain more than three times each day was synonymous with checking "as needed." Twenty percent selected three times per day; one selected twice.

Drawing on a variety of experiences, forty percent of authors strongly believed post-operative analgesia guidelines to be both adequate and properly enforced while only slightly fewer agreed with less conviction. A few researchers disagreed, but none did so with vehemence. Thus, overall, the system was given approval with eighty percent in agreement.

No one denied the importance including any use or omission of post-operative analgesia in published reports, though most did not feel strongly in favor, and two of the ten selected "not applicable." Forty percent said unpublished procedures were adequate, while half that number disagreed. Thirty percent had no appropriate experience.

Regarding the accuracy of post-op analgesia reported in published articles, this group divided evenly. Forty percent stood on each side of the issue, offset only by one person in strong agreement of report accuracy. Ten percent did not have a basis for response.

Half of the authors said information regarding survival of animal models or post-operative analgesia was left out of articles due to irrelevance. The other half either had original answers or no response. One "original" answer was that information should only be included if relevant, which seems very similar to the sentiment of those who chose irrelevance. A slight majority, sixty percent, agreed such information should be published, regardless of relevance. Strong agreement and plain disagreement were both selected by twenty percent.

Forty percent of these authors indicated local IACUC members should define post-operative analgesia guidelines. Half selected attending veterinarians, and twenty percent believed in the discretion of the researcher. One response, which happened to originate in a foreign country, suggested ethic committees enforce internationally accepted procedure.

Survey for Periodical Research Authors

1. Years of experience with experiments involving canine models:
a. (1-5) b. (6-10) c. (11-15) d. (16+)

2. The treatment of pain is as important for canines in laboratory experiments as it is for canines in clinical veterinary settings.
a. Strongly agree b. Agree c. Disagree d. Strongly Disagree

3. It is important to provide post-operative analgesia, if the nature of the experiment renders it possible.
a. Strongly agree b. Agree c. Disagree d. Strongly Disagree e. N/A
If c. or d., please continue to question 6.

4. After surgical procedures, dogs should be assessed for pain using:
a. More objective methods, such as the use of an algometer
b. Subjective methods, such as a visual assessment
c. Both
d. Neither. Please Explain_____

5. During recovery from surgical procedures, checking for pain "as needed" means:
a. Once every day b. Twice every day c. Three times per day d. More Often

6. In my experience, policies regarding post-operative analgesia are adequate.
a. Strongly agree b. Agree c. Disagree d. Strongly Disagree e. N/A

7. In my experience, policies regarding post-operative analgesia are enforced.
a. Strongly agree b. Agree c. Disagree d. Strongly Disagree e. N/A

8. It is important for researchers to report any use or omission of post-operative analgesia in their publications.
a. Strongly agree b. Agree c. Disagree d. Strongly Disagree e. N/A

9. In my experience, any unpublished use of post-operative analgesia has been consistently adequate.
a. Strongly agree b. Agree c. Disagree d. Strongly Disagree e. N/A

10. In my experience, researchers accurately report their uses of post-operative analgesia in published articles.
a. Strongly agree b. Agree c. Disagree d. Strongly Disagree e. N/A

11. Factors that discourage the publication of information such as the survival of the animal models or any post-operative analgesia include:
a. Irrelevance b. Word Limits c. Time Restrictions d. Other. Please explain_____

12. Journals should have a position statement requiring authors of original research to report their post-operative care, regardless of relevance to the goal of the experiment.
a. Strongly agree b. Agree c. Disagree d. Strongly Disagree e. N/A

13. Guidelines for post-operative analgesia should be defined by:
a. local IACUC members b. Attending veterinarians c. Federal agencies (USDA, NIH, etc.) c. Researcher d. Other. Please explain_____

I would like to receive a copy of this completed project.
a. That would be great. b. No thanks.

Figure II: Survey for Journal Research Authors

Question	Response				
	A	**B**	**C**	**D**	**E**
1	*j*	*g*	*efik*	*acdh*	
2	*adefghijk*	*c*	X	X	
3	*adefghjk*	*c*	X	i	
4 (α)	X	*adh*	*cefgik*	X	
5 (α,β)	X	*a*	*cg*	*defhik*	
6	*dfgk*	*aeh*	*ci*	X	
7	*dfgk*	*aceh*	*i*	X	
8 (β)	*i*	*cdefgk*	X	X	*ah*
9 (α)	X	*fghk*	*cd*	X	*aij*
10 (α,β)	*k*	*adgh*	*cdfi*	X	*j*
11 (α,β)	*fghij*	X	X	X	
12	*ik*	*acefgj*	*dh*	X	
13 (α,β)	*aefh*	*acdfg*	*fk*	X	
Project copy?	*acdefi* (yes)	*gkj* (no)	X	X	

Table IV: Journal research author survey responses. Eleven responding researchers are designated as *a* through *k*. Answers not selected in any survey are labeled X. Omitted responses or question-mark answers are indicated with α, while β indicates written comment. Blank portions, such as the space in column E, represent answers not given as an option on this survey. Further detail can be found in the text, under Research Author Survey Results, on page ten.

Question	% Researchers Selecting Each Option				
	A	B	C	D	E
1	10	10	40	40	
2	90	10	X	X	
3	80	10	X	10	
4	X	30	60	X	
5	X	10	20	60	
6	40	30	20	X	
7	40	40	10	X	
8	10	60	X	X	20
9	X	40	20	X	30
10	10	40	40	X	10
11	50	X	X	X	
12	20	60	20	X	
13	40	50	20	X	
Project copy?	60 (yes)	30 (no)	X	X	

Table V: Percentages of responding researchers who selected each answer. X indicates options never selected. For comparison, the one blank survey was disregarded, leaving a total of ten responses.

Note: In two instances, more than one response was marked for a single question. Other answers were original or omitted, reducing the number of circled responses. As a result, this graph simply shows whether options were favored or disfavored by most researchers. The percentages given for the responses to each question will not add up to one hundred percent.

3.3 Influence of Publication Process

The checklist used in the review process was requested from both journals reviewed in this study. Each responded, providing not only the checklist but also supplemental information. This additional material was easily used to compare attitudes of human medical versus veterinary medical journals. The review checklist and guide for authors provided by *Anesthesia & Analgesia* is located in Appendix C. Appendix D consists of the checklist from the *American Journal of Veterinary Research* (*AJVR*),

AJVR's cover letter, guidelines for peer reviewers, and an additional editorial regarding responsible care of research animals.

3.4 IACUC Survey

IACUC members from local institutions were surveyed regarding general attitudes toward post-operative care of animals. See Figure III for survey questions. Figure V contains demographic results, and questionnaire results are reviewed in Table VI.

Forty questionnaires were sent out to local IACUC members. Eight were returned. Responses to demographic questions yielded a diverse range of people. All those surveyed reported themselves to be IACUC members.

Researchers were the largest category of responders, representing nearly thirty-eight percent. Twenty-five percent were administrators, while investigators and technicians each represented just under thirteen percent of the entire group.

Overall, the subjects surveyed were quite experienced in their fields. All of them had at least six years of experience, and half were between six and ten years. A substantial group, almost thirty-eight percent, had experience ranging over more than fifteen years. Significantly, three quarters of those surveyed reported a history of working with laboratory canines.

The first group of survey questions dealt with the care of laboratory animals. For each of these questions, Strongly Agree was the unanimous response. The next four questions moved on to the subject of post-operative analgesia. With the exception of those who answered N/A (not applicable or no answer) each person gave a response of

Agree or Strongly Agree. The final question of this set concerning post-operative care questioned the frequency at which recovering animals should be provided with analgesics. While thirty-eight percent of the group disagreed post-operative analgesia should only be given "as needed," the remaining sixty three percent felt post-operative analgesia "as needed" was sufficient.

The next set of questions targeted current policies regulating the care of laboratory animals. These were directed toward the enforcement of such policies at each subjects' institution. While no one disagreed that their institution was enforcing these policies, thirteen percent felt policies could be more strictly enforced and even improved upon.

The final group of questions concerned material published in scientific journals. Subjects were asked if they regularly read or reviewed original research. Sixty-three percent of the group gave affirmative replies. Their responses were used exclusively to calculate percentages for questions eleven through fifteen.

Questions eleven through thirteen dealt with the extent of post-operative analgesia use. All respondents agreed on the importance of researchers reporting any use of post-operative analgesia. Sixty percent felt this reflected the present situation. Twenty percent, however, noted a lack of reporting of pain management. Next, forty percent agreed the use of post-operative analgesia was sufficient, though unreported, while twenty percent felt analgesia was not used at adequate levels.

Question 14 investigated the effects of limitations placed on articles by journals. While twenty percent felt these limitations restricted the reporting of pain management, forty percent reported they had no bearing. The final survey question assessed attitudes

regarding the idea of journals having a position statement requiring authors of original research to report post-operative care regardless of relevance. While sixty percent of respondents felt this was a beneficial suggestion, twenty percent thought it was unnecessary.

Figure III: Survey created for local IACUC members.

Demographics: Please Circle All That Apply

Profession/Position:

(a) Researcher (b) Technician (c) Administrator (c) Investigator (d) IACUC member

Years in Field:

(a) 1-5 (b) 6-10 **(c)** 11-15 **(d)** 16+

Do you now or have you ever worked with laboratory dogs?

Questionnaire:

For each question, do you (a) Strongly Agree, (b) Agree, (c) Disagree,

(d) Strongly Disagree, or (e) Have no basis for an answer?

(a b c d e)

1. It is important to insure the proper treatment of research animals. (a b c d e)

2. The treatment of laboratory dogs should be held to the same standards as any other laboratory animal. (a b c d e)

3. The treatment of pain is as important for research dogs as it is for clinical veterinary patients. (a b c d e)

4. After surgical procedures, dogs have additional requirements for care compared to their regular husbandry needs. (a b c d e)

5. After surgery, research dogs should be checked more than twice a day.

(a b c d e)

6. It is important to provide dogs with post-operative analgesia. (a b c d e)

7. Post-operative analgesia should be provided on an "as needed" basis.

(a b c d e)

8. Policies at my institution regarding post-operative analgesia are enforced.

(a b c d e)

9. Policies at my institution regarding post-operative analgesia should be more strictly enforced. (a b c d e)

10. Policies at my institution concerning post-operative analgesia should be improved upon. (a b c d e)

Do you regularly read or review original research in scientific journals?

If so, please continue to Question 11.

11. It is important for researchers to report their uses of post-operative analgesia in their publications. (a b c d e)

12. Presently, researchers accurately report their use of post-operative analgesia in published articles. (a b c d e)

13. The use of post-operative analgesia in research animals is presently adequate although not reported in publications. (a b c d e)

14. Journal guidelines (word limits, time pressures, relativity to study, etc.) hinder the researchers' ability to report the use of post-operative analgesia and other refinement techniques. (a b c d e)

15. Journals should have a position statement requiring authors of original research to report their post-operative care, regardless of relevance. (a b c d e)

	Strongly Agree	Agree	Disagree	Strongly Disagree	N/A
1. It is important to insure the proper treatment of research animals.	100%	0%	0%	0%	0%
2. The treatment of laboratory dogs should be held to the same standards as any other laboratory animal.	100%	0%	0%	0%	0%
3. The treatment of pain is as important for research dogs as it is for clinical veterinary patients.	100%	0%	0%	0%	0%
4. After surgical procedures, dogs have additional requirements for care compared to their regular husbandry needs.	75%	25%	0%	0%	0%
5. After surgery, research dogs should be checked more than twice a day.	25%	50%	0%	0%	25%
6. It is important to provide dogs with post-operative analgesia	75%	13%	0%	0%	13%
7. Post-operative analgesia should be provided on a "as needed" basis.	25%	38%	38%	0%	0%
8. Post-operative analgesia policies are enforced at my institution.	63%	25%	0%	0%	13%
9. Policies at my institution regarding post-operative analgesia should be more strictly enforced.	0%	13%	25%	0%	63%
10. Policies at my institution concerning post-operative analgesia should be improved upon.	0%	13%	50%	13%	25%

Do you regularly read or review original research in scientific journals? Yes 63%

Only those who answered Yes completed Q11-Q15 No 38%

	Strongly Agree	Agree	Disagree	Strongly Disagree	N/A
11. It is important for researchers to report their uses of post-operative analgesia in their publications.	60%	40%	0%	0%	0%
12. Presently, researchers accurately report their use of post-operative analgesia in published articles.	20%	40%	20%	0%	20%
13. The use of post-operative analgesia in research animals is presently adequate although not reported in publications.	0%	40%	20%	0%	40%
14. Journal guidelines (word limits, time pressures, relativity to study, etc.) hinder the researchers' ability to report the use of post-operative analgesia and other refinement techniques.	0%	20%	20%	20%	40%
15. Journals should have a position statement requiring authors of original research to report their post-operative care, regardless of relevance.	40%	20%	20%	0%	20%

Table VI: Survey results generated by local IACUC members from both academia and private corporations. Percentages reflect information from a total of eight responses.

4. Discussion

4.1 Summary

The purpose of this study was to review the current system of regulation of post-operative analgesia use in laboratory canines. All areas of the structure were examined at both the institutional and the individual level.

The transition from completed study to published material was investigated through published articles in *Anesthesia and Analgesia* and the *American Journal of Veterinary Research.* Those involving certain surgeries on dogs were examined in both journals. Differences between human medical journals and veterinary journals were noted.

Part of the study concentrated on the regulatory system. Two questionnaires were formed and distributed to assess policies and procedures. The data collected was then reviewed, recorded, and quantified.

Following the analysis of collected data; it was the aim of this project to suggest improvements for the current regulatory system that would help ensure productive welfare measures and more productive reporting of post-operative care.

4.2 "Anesthesia and Analgesia"

Background

Anesthesia and Analgesia is the journal of the International Anesthesia Research Society, Society of Cardiovascular Anesthesiologists, Society for Pediatric Anesthesia, International Society for Anesthetic Pharmacology, and Society for Technology in Anesthesia. In particular, the International Anesthesia Research Society (IARS) owns and publishes this journal. IARS is an apolitical, not-for-profit medical society founded

in 1922 "to foster progress and research in all phases of anesthesia." (intl.anesthesia-analgesia.org) The current IARS mission Statement is: "To improve the practice of perioperative medicine throughout the world by the creation and dissemination of medical knowledge in anesthesiology, pain management, intensive care, the related clinical practices and pertinent basic sciences."(www.iars.com)

The circulation of this periodical is geographically diverse and extensive; the IARS alone has 14,000 members worldwide. *Anesthesia and Analgesia Online* has a service contract to bring up the connection speeds of subscribers in Australia, Brazil, China, France, Germany, Hong Kong, Ireland, Israel, Italy, Japan, Mexico, Russia, Singapore, South Africa, South Korea, Spain, Sweden, Switzerland, Taiwan, The Netherlands, and the UK (intl.anesthesia-analgesia.org). Despite the massive audience, *Anesthesia and Analgesia* is loosely geared toward specific health professionals. Most members/subscribers have doctoral degrees, such as MDs, DVMs and PhDs. There are also membership categories for residents in training and for associate members from the allied health professions.

Research Publication

This journal is published once a month with an average of fifty articles per issue. In 1999 and 2000 combined, almost 150 experiments involving canines were published in *Anesthesia and Analgesia.* The majority of experimental surgeries were thoracotomies, followed in frequency by craniotomies, which were not included in this study. An overwhelming majority of the surgeries ended in euthanasia, excluding them from this study. Relevant articles originated from diverse settings that included Europe, Asia, South America, North America, and Australia.

The numbers of experimental animals in *Anesthesia and Analgesia* varied from large groups, such as n=46 to smaller ones, like n=6. Typically, European experiments involved more conservative numbers of animals. Fewer animal models are generally associated with a more refined experiment. American experiments involved both ends of the spectrum. In general, Asian experiments frequently involved large numbers. However, the number of models cannot be evaluated appropriately without information as to how many animals are necessary to achieve a particular result. If too few animals are used to obtain significant data, then the experiment may not have sufficient credible results. Such a situation would be extremely wasteful, or course. The idea that larger control and experimental groups are perhaps the result of testing many techniques or substances at once should also be considered.

Reports of Pain Management

Of the four appropriate articles reviewed for this study, only one mentioned use of post-operative analgesia. The only type of procedure with reported use of pain management was thoracic surgery. This is expected, as surgeries involving the thorax are considered the most painful. It was surprising, however, that among two other thoracic and one stifle procedure no analgesia was reported. Only that single article, one of three thoracic procedures, contained evidence of pain regulation.

Again, one reason for this lack of reporting post-operative care could be a lack of administration. Pain medication may interfere with the purpose of the study, or the difficulty could simply be that the staff and researchers lack awareness of and familiarity with signs and treatments for pain.

A second possibility as to why pain management was not reported in *Anesthesia and Analgesia* is the strict word limits this journal imposes on submitted articles. As seen

in Appendix C, each type of manuscript has a different word limit as well as a limit to figures and graphs. If post-operative pain care is not crucial to a study, it could easily be left out of a report to save space.

Also, this particular journal requires a written statement of IACUC approval in every article. Also according to Appendix C, there must be a statement from the author's institutional animal investigation committee in the text of the article before *Anesthesia and Analgesia* will consider accepting it. Many times this could be considered a worthy substitute for a proper description of animal care. This could especially be true in those articles that claimed they followed secondary guidelines, for example the American Physiological Society's guidelines, on the care of animals.

4.3 "American Journal of Veterinary Research"

Background

The *American Journal of Veterinary Research* is a peer reviewed scientific journal published monthly by the AVMA. Articles are submitted by DVMs, MDs and PhDs for the purpose of reporting the, "highest quality research that [has] clear potential to enhance the health, welfare, and performance of animals."(www.avma.org/publications/ajvr/ajvr_ifa.asp)

Reports of Pain Management

Roughly 240 articles are published per year and of the 480 articles published between the years 1999 and 2000, 19 fit the inclusion criteria for this study. Of these, a low twenty-six percent reported the use of post-operative analgesia. The distribution of the breakdown of which types of surgeries reported use of analgesics was very unbalanced. This gives an indication of potential inadequacies of treatment. Because

thoracotomies are considered at the top of the list of moderate to severely painful procedures, it was expected that studies involving thoracotomies would have the highest percentage of reported use of analgesics(Karas 2000). However, only two out of the six articles describing thoracotomies reported the use of analgesia while for those involving hip surgeries, 50% of articles reported analgesics. In addition, we found that none of the articles concerning abdominal or knee surgeries reported any use of post-operative analgesia. Though not every abdominal procedure is considered severely painful, all orthopedic and limb surgeries are and would therefore warrant the use of analgesics(Karas 2000).

In speculation as to why post-operative analgesics were not reported in these articles, several possibilities exist. A simple lack of analgesia use is the most obvious suggestion. If accurate, it's evidence of an important breakdown in the intent and processes of regulatory principles and IACUC function. Secondly, analgesic use may have been withheld intentionally. There are certain circumstances under which the withholding of post-operative analgesics is permissible. This occurs when the use of analgesia will compromise the results of the study. In this case it must be adequately justified to the IACUC and the study identified as category E. A category E study is one that included the use of, "animals involved in procedures which cause pain or distress that was not relieved by drugs for scientific reasons." All other studies that cause pain on their animal models must use some method of pain management and relief(www.aaalac.org/html/about.html).

Yet another reason some articles may not report the use of post-operative analgesia is that full details of animal care were not reported due to author decision or

oversight or due to word limits placed on submitted manuscripts. The latter would be unlikely to be a factor for the *AJVR* as this journal does not have a set page limit for its publications and therefore does not limit the number of words per article. *Anesthesia and Analgesia* has a strict word limit according to article type, which can be seen in Appendix C.

Also, some journals require a written statement of IACUC or similar agency approval in the submitted articles. In order to save space, the author might mistake this statement of IACUC approval as sufficient explanation of the proper treatment of animals. This may be so especially in the cases where IACUC approval is the only requirement regarding the care and treatment of animals, which is also the criteria for *Anesthesia and Analgesia* articles. If it is not a journal requirement and it does not have direct relevance to the results of the study, authors may be inclined to leave out this important information. For this exact reason AJVR does not require statement of IACUC approval. "Such a statement does not, in and of itself, provide sufficient information about the care experimental animals received and is not a substitute for a full description of the care of the animals used in the study."(Matushek, 2001)

Therefore, more thorough reports of measures ensuring animal welfare, such as post-operative pain management, should not be excluded from the text of *AJVR* articles due either limited space or the presence of similar, inadequate information. In fact, *AJVR* publishers have taken specific care to encourage article text containing this information.

These facts imply that any lack of publication is due to the actions of authors. However, eighty percent of surveyed research article authors supported inclusion of this information regardless of relevance to the published experiment.

Reality obviously does not reflect statements given by *AJVR* authors and publishers, with an average of less than thirty percent of articles reviewed addressing the welfare of laboratory animals. (Table III.) Interestingly, authors and publishers alone have influence over the material in published articles; responsibility is theirs alone. In conclusion, though *AJVR* had far more data on humane measures, such as post-operative analgesia administration, than *Anesthesia and Analgesia*, information given by authors and publishers reveal this percentage to fall short of its potential, without any reasonable explanation.

4.4 Journal Comparison

Though slight, difference exists between the rates of reported analgesia in *Anesthesia and Analgesia* and *AJVR*. When looking at the percentages of reported use of post-operative analgesia, Table III, there is only a 3% difference between the two journals, *Anesthesia and Analgesia* with 25% (1 of 4 articles) and *AJVR* with 28% (5 of 18 articles). However, when the magnitudes of the journals are considered, this becomes a large difference. Of the average 240 articles per year, giving 480 articles over a two-year span, *AJVR* had five reports of the use of post-operative analgesia in experiments using canines. *Anesthesia and Analgesia* publishes an average of 600 articles a year, making their two year total 1,200 articles, and of these 1,200 articles only one made any mention of the sue of post-operative analgesia. When these facts are brought into context the difference becomes staggering.

Both journals that were reviewed were contacted and information regarding the peer review process was requested. Both journals responded with the requested reviewer's checklist and additional information. Though they both provided information,

the journals' attitudes concerning our research was apparently different. *Anesthesia & Analgesia* replied by sending the reviewer's checklist, as requested, and supplementing it with their Guide for Authors, which is easily accessible from any of their journals as well as their web site. Their reply consisted of these two items and a post-it note reading "per request." *AJVR* however gave a much more interested and elaborate response. Included in their reply was a cover letter expressing their thanks for our interest in their journal as well as an invitation for future contact. In addition to the reviewer's checklist and the guidelines for reviewers, they sent an editorial concerning the topic of responsible use of animals in research. The editorial expressed the journal's call for not only responsible treatment of animals but also for the responsible reporting of this care. This paper also told how the journal itself regulates the publishing of articles, postponing those articles in which treatment of animals is questioned until the authors clear up any discrepancies. These extra items showed the genuine concern of the *AJVR* as well as the American Veterinary Medical Association (AVMA), who publishes the *AJVR*, for the care and welfare of laboratory animals.

The content of the information sent also differed between the "veterinary journal," written by veterinarians for veterinarians and the "human journal," written by medical doctors for doctors. The first noticeable point is that the checklists are extremely different in length and detail. The *Anesthesia and Analgesia* checklist is very brief asking only one question each about the scientific validity, importance, interest to readers, originality and presentation. All of these points are covered in just the Overview section of the *AJVR*. The *AJVR* also asks reviewers to judge the specifics of the manuscript. Most relevant to this study is the Materials and Methods section of the *AJVR* checklist. When

reviewing the Materials and Methods for a manuscript the reviewers are asked if there is any doubt that the animals were treated humanely. The *Anesthesia & Analgesia* checklist makes no mention of the Materials and Methods at all, let alone the treatment of animals used in the study.

In addition to the reviewer's checklist, both journals provided information regarding author requirements for article submission. There were two major differences between the two journals' Guide to Authors. First, *Anesthesia & Analgesia* requires that any submitted text include a statement regarding IACUC approval. On the other hand the *AJVR* does not require that the authors indicate that their study was approved by the presiding IACUC. Their reasoning behind this is because, "such a statement does not, in and of itself, provide sufficient information about the care experimental animals received and is not a substitute for a full description of the care of the animals used in the study." This is an interesting statement because it shows that even this journal recognizes a weakness in the system of regulation of the care of research animals.

The second major difference between the authors' guidelines of the two journals has to do with restrictions. The *AJVR* stated that they do not have any specific page limits for their journal and therefore do not put any strict limits on the lengths of the articles submitted. This limitless structure would give an author plenty of opportunity to discuss the methods of his/her research, even the treatment and care of their animal models. *Anesthesia &Analgesia* however does impose very specific and strict word limits. Each type of publishable article or report has a different word limit. A general article has a limit of 3000 words, these articles describe any clinical or laboratory investigations. In the case of research whose main focus is not the care and treatment of

pain in animals, it would be possible for the details of the animals to be edited out in order to conserve words. It is limitations like these that hinder the authors' ability to report the care of their animals. When reporting of certain information is not required and the authors are limited to what they can report, editors and peers can never properly review it and cases of improper treatment of animals could go unnoticed.

In addition to the statistical differences, it is clear from both the manner of response from each journal as well as its content that veterinary medical journals take more interest in the care and use of laboratory animals. Because of the extra attention veterinary journals pay to this subject, they play a larger and more effective role in the regulation of the care and treatment of research animals.

4.5 Survey for Research Article Authors

As mentioned previously, exactly half the research author surveys generated some response. However, survey a few obstacles existed regarding survey response.

Most researchers surveyed are faculty at universities in the United States or other developed nations. Assuming their daily schedules are similar to the hectic agendas of local professors, fifty percent seems like an excellent level of response. Secondly, these surveys were completed despite any misgivings stemming from the idea they were tools of animal rights' activists. Although contrary to the letter mailed with the survey, such concern would seem reasonable.

In addition, efforts to return these surveys were not a response to any tremendous incentive. Half of the surveys returned indicated no interest in the available copy of this finished project. Therefore, half of the information came from respondents who saw absolutely no incentive. The fact that one took the time to return a blank survey supports

the idea that some authors are very concerned about constructive investigations regarding this subject. One author in South America could not use the United States postage on the included self-addressed response envelope. The researcher not only completed the survey but also took the time to find a fax number and return it that way.

For these reasons, it may be assumed that research article authors are interested in doing what they can for the cause of research animal welfare. Their effort without any reward indicates a willingness to ensure constructive studies can be done in this area.

It seems promising that so many authors said the welfare of animal models and analgesia administration was so important. Indicating so many daily checks were necessary is not a small commitment of time, especially with large groups of canine models. This further indicates an average researcher would put effort into ensuring the comfort of post-operative animal models. If surveys were answered accurately, any gap in the regulation system would not be due to dispassionate scientists.

Eighty percent said current guidelines were acceptable, but half of them said reports of analgesia in published articles were not accurate. Since so many researchers said animal welfare was important and, at the same time, that guidelines were acceptable, perhaps this indicates a lack of publication does not mean no analgesia was used. It is not reasonable to assume researchers consider welfare important while claiming guidelines permitting painful surgeries with no analgesia are acceptable.

This survey revealed a strong minority that considers post-operative analgesia irrelevant information. However, eighty percent would like to see such information included in all articles regardless of relevance. Considering this group's interest in animal welfare, this may indicate that when specific analgesia information is necessary

for publication, it may be be administered with more care. When taking the level of effort a majority of researchers seem willing to put into animal welfare, such a requirement should not meet tremendous resistance.

The varieties of response concerning the origin of guidelines strengthen the idea that there is no obvious solution to gaps in the system. At the same time, if one organization currently had effective, direct responsibility, that organization would have been indicated here by most of these researchers. Fortunately, due to the uncertainty evident in the wide distribution of response, perhaps scientists would be very willing to comply with whichever organization seems the most effective after policy revision.

4.6 IACUC Questionnaire

This study focused exclusively on research involving laboratory canines. Therefore, verification of such experience was a crucial part of the questionnaire. Seventy-five percent of returned surveys reported experience with dogs, assuring survey response relevancy due to the adequate and proper experience of these particular IACUC members. Another positive demographic was the number of researchers represented, which constituted nearly thirty-eight percent of the overall response. These subjects are nearly ideal, with their knowledge and understanding of IACUC goals and procedures as well as their firsthand experience with the circumstances and processes surrounding actual research. In addition, members of the surveyed group possessed extensive experience, almost thirty-eight percent having more than fifteen years of experience. This fact lends further credibility to survey results, as these people have undoubtedly dealt with a number of situations that may be relative to this survey. Overall, survey

results indicated a substantial part of the surveyed group consisted of experienced scientists who had direct contact with laboratory dogs. These demographics strongly indicate that this is an appropriate group to contribute insight on attitudes toward and reporting of any use of post-operative analgesics.

As previously stated, the first group of questions investigated the care of laboratory animals. These questions were designed for Strongly Agree to be the answer reflecting the most positive supportive view of the treatment of animals. The unanimous Strongly Agree response suggests all who were surveyed view the general good treatment of laboratory animals to be significantly important.

This pattern held true for the next section of questions, which were also designed for Strongly Agree to reflect the most supportive view of the proper treatment of animals. Generally, responses indicated that post-operative analgesia is regarded as an important factor in the treatment of laboratory dogs. A logical view on this matter is that any pain treatment should be given on a set schedule, regardless of any apparent wellbeing of the animal, because pain is extremely difficult to assess. Unfortunately, the majority did not share this view. A disappointing sixty-three percent of those surveyed felt that post-operative analgesia given on an "as needed" basis was sufficient. This opinion could be a result of the lack of knowledge of pain and pain management.

The next set of questions targeted the policies currently in place. As expected, the majority felt their institution properly enforced suitable regulations concerning post-operative analgesia. Comments in response to this survey were mainly directed toward this question, Question 10. Those who commented stated that while their institutions' policies were adequate, any system over time can be improved upon.

The final section of questions dealt with the information published in scientific journals. Everyone surveyed agreed that publishing information about post-operative analgesia was important. Most felt it was adequately presented in journals. However, a portion, twenty-percent, felt the use of postoperative analgesics were not being reported adequately. While this is a small percentage, it does confirm the existence of a portion of scientific community who feel the reporting of the use of post-operative analgesics is a problem that should be addressed. While this concern is not prominent or highly publicized, it remains, and should certainly be addressed.

When questioned regarding any lack of reporting of pain management in scientific articles, those surveyed did not feel word limitations imposed by editors were the cause. This response was expected, because many of the people surveyed were from an academic veterinary setting. As discussed above, *AJVR*, a journal which is commonly their most prominent representation in the periodical media, does not impose such restrictions. The majority, however, felt it would be beneficial for each journal to require authors to report their use of post-operative analgesia. A less significant number, twenty percent, disagreed with this suggestion. Perhaps reluctance to consider change is due to the possibility of inconvenience added to the already significant paperwork required to carry out a study using animal models.

Overall survey responses were as expected. Unfortunately, no response was received from either of the two Biotech companies surveyed. One firm reportedly refused to distribute the survey, claiming it could be a source of information used against business actions targeted by some extremist animal rights groups. This is a reasonable

and expected response from a type of company that frequently receives negative press from such activists.

4.7 Possible Project Improvements

After gaining project experience, it's clear many changes could have been made to experimental design to ensure a more thorough report. A different species, one involved in a greater number of studies, would have facilitated data collection, yielding a greater number of relevant articles.

Also, the two journals involved in this study might not have been a proper representation of their respective portions of the medical community, veterinary medical and human medical. If additional journals were reviewed, a more accurate impression of each field would have been evident.

Also, journals may have been inappropriate for other reasons. For instance, the human journal dealt with an overwhelming majority of lethal procedures, excluding reports from this study. A different human medical publication might have encompassed a greater variety of experimental procedures or focused on more experiments without death as an endpoint.

In addition, this project would have been more extensive after reviewing a greater number of journal issues, involving more articles and yielding a larger range of data. This would be accomplished by reviewing more than two years of publications. Data spread over more than two years may be observed to change from year to year. Perhaps more post-operative analgesia is reported this year in comparison to reports written five years ago. Did the initiation of certain laws, such as those in the introduction

background, have a significant effect on the way research was conducted? Such information would add to the scope of our study.

Human and veterinary medical journals could have been compared subjectively through surveys as well as objectively through article content. Regulatory effectiveness could have been assessed more generally. IACUC members from outside the local area could have been surveyed. All IACUC surveys could have contained questions encompassing the subject's entire range of experience, instead of their institution's current procedures exclusively. It would have been interesting to assess public response to the suggestions presented by this final paper.

Had the questionnaire been worded differently, it might have elicited a greater number of responses. IACUC questions regarding policies of each individual's institution may have been too personal. Such invasive questions may be responsible for the lack of response from biotechnology companies. Survey questions should have been worked more generally, citing the government as the main institution. This would have relieved fears that the survey would be used for alternate purposes, such as animal rights activism. An incentive of any kind may have enhanced the level of response.

Finally, a copy of this finished project should not have been promised as a response anonymous author surveys. After responses left the mailing envelopes, the surveyed individual could not be identified.

Even with the limitations recognized here, several conclusions can be drawn which could be further tested in a subsequent study. Plus, errors in the design of this study can prevent similar errors in further studies, ensuring greater efficiency.

5. Conclusion

5.1 Suggestions

After reviewing the system currently in place, several suggestions can be made. They are illustrated in Figure VII. A large gap in the post-operative care of animals seems to be a result of a lack in knowledge of pain recognition and management. This occurs due to researchers and their staff as well as those who regulate the system.

As stated earlier, pain is difficult to assess. If pain is not recognized in the first place it cannot be properly cared for. For this reason, it is suggested that laboratory technicians, the people who have direct contact with the animals, be better trained and be provided a better collection of available resources on identifying and managing pain. If the technicians were more adept at recognizing and treating pain and distress, less suffering would go unnoticed.

The IACUC monitors all experimental activity that involves the use of all and any live vertebrate animals. However, more must be done in addition to the initial project approval. While the IACUC does review any ongoing research one a year, IACUC members should also conduct "spot checks" of all of the active experiments. This would eliminate the possibility that an approved procedure had been changed putting the animals' welfare in danger. In order for this process to be totally effective, IACUC members involved in these checks must be properly trained, in the same manner as the technicians. IACUC members checking research conditions should be able to recognize pain and distress, as well as make suggestions to alleviate it. Once the pain had been recognized, there should be a person involved in the study or its regulation who can classify the pain and give scientific suggestions on how it should be managed. The

overseeing veterinarian would be the best person for this position. This doctor should be required to have more than a general knowledge of anesthesia and analgesia.

The next suggestion on improving the regulation of animal care targets the journals. Currently there is only the requirement that the submitted paper mention IACUC approval. However this is not proof that the IACUC has in fact given approval for that specific project. For this suggestion, a system of regulation has been borrowed from the granting agencies. Projects will not receive money from a granting agency without written IACUC approval. In the same respect journals should require a copy of IACUC approval upon submission. This would not be a difficult change to make. It should be made that authors must include, with their manuscript, a copy of all protocols that were submitted to and approved by their IACUC.

As discussed in Appendix B, there is no standard procedure for the assessment and measurement of pain and distress in an animal. Although new techniques like the use of an algometer are being designed and improved upon, more work needs to be done. The government as well as voluntary and privately funded organizations should encourage research into pain and how to properly detect and relieve it. If better systems of recognizing pain were present the treatment of this discomfort would be much simpler. In the same respect there is no official standard set of analgesics for any one procedure. As suggested by Dr. Alicia Karas, common surgeries should be looked at and the pain and discomfort they cause assessed. Then using knowledge of proper pain management, a list of minimum analgesics per procedure could be compiled. This would at least provide a minimal universal standard for the treatment of painful procedures (Karas, 2000). All surgeons and researchers, regardless of their anesthetic and analgesic

background would have a base of core information guiding their use of post-operative analgesics.

Figure VII
Current Path for the Regulation of the Care of Laboratory Animals
With Suggestions for Improvement of Regulation

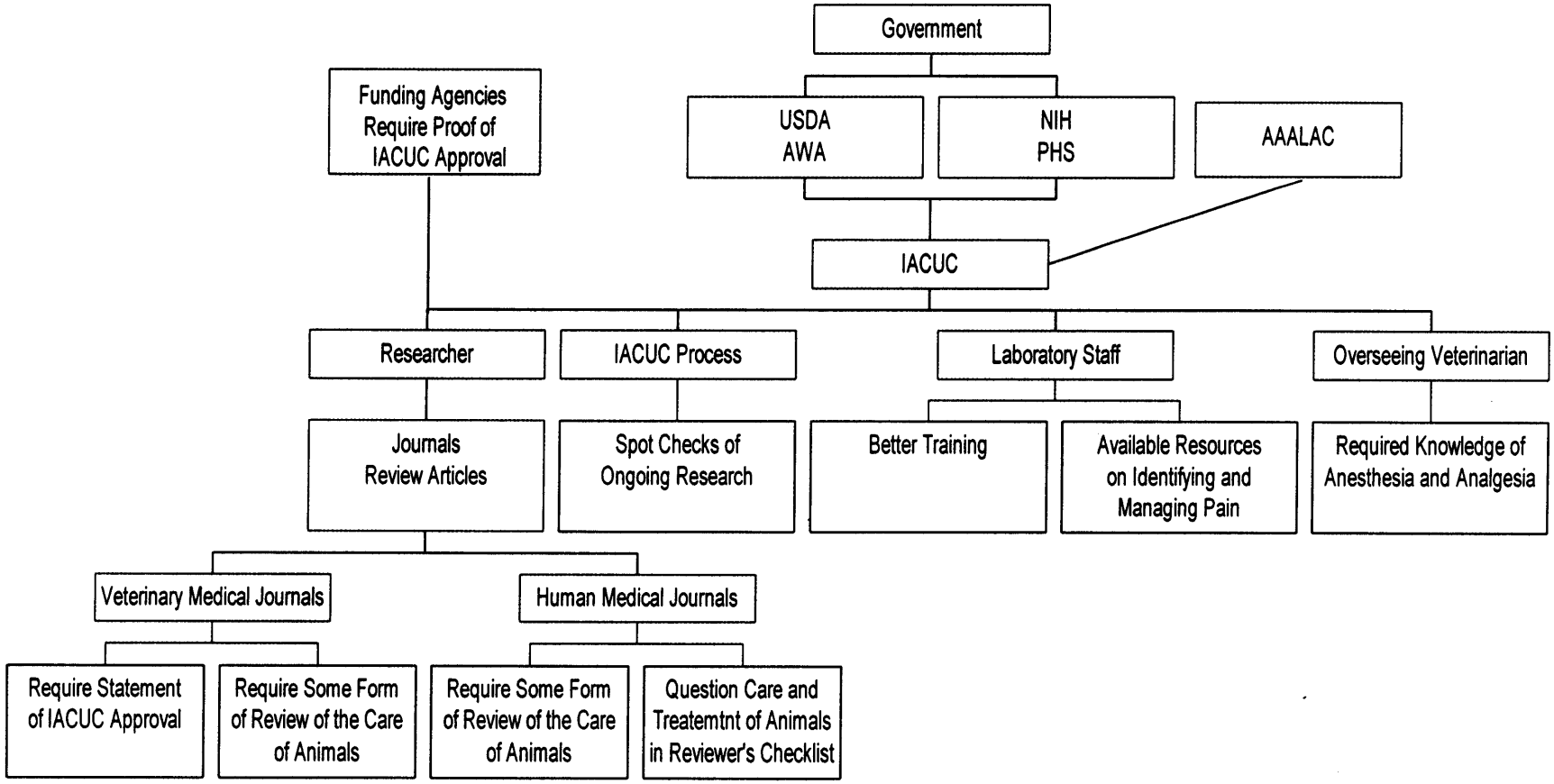

Figure VII: Current Path for the Regulation of the Care of Laboratory Animals with Suggestions for Improvement of Regulation

The section of the flow chart consisting of the blue boxes connected by the black lines represents the current pathway for the regulation of the care of laboratory animals. The government is divided into two subsections, the United States Department of Agriculture (USDA) and the National Institutes of Health (NIH). The USDA is the agency that put the Animal Welfare Act (AWA) into effect and the NIH controls the Public Health Services (PHS). In addition to the government organizations there is Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC), a volunteer program that give certification to institutions that show proper care and use of laboratory animals. All of these groups and their policies control the guidelines set forth for the individual Institutional Animal Care and Use Committee (IACUC). In turn the IACUC sets specifications for the IACUCs own regulation process, the veterinarian who oversees the specific research project, the primary investigator (researcher) who runs the study as well as the laboratory staff. The Next form of regulation happens when the completed study is submitted to a scientific journal for publication. The journal reviews the article and insures that it states the guidelines followed and IACUC approval if relevant.

The black boxes connected to the current regulations by red lines represents the suggestions that this paper is making. In order for the animals to get better care, the laboratory technicians must have better training and more resources available to them to aid in their recognition and treatment of pain and distress. The IACUC members must also have similar proper training. It is suggested that the overseeing veterinarian be required to have some familiarity with anesthesia and analgesia to better assist the primary investigator. Finally veterinary journals should add a level of regulation to their review process by requiring proof of IACUC approval. Human medical journals need to add sections to their reviewer's checklist questioning the treatment of animals. Also the journals should incorporate some form of review of the care of the animals in their peer review system.

5.2 Summary

It is clear from the presented data that weaknesses exist in the current regulation of post-operative procedure for laboratory canines. Laws are put in place to ensure proper treatment of animals; this includes pain management. If animals are not treated properly, if their pain is not recognized and relieved, then the system should be changed at the highest level possible, the government organizations. Such changes would call for the refurbishing of the current legislation. These actions could potentially take years, if any change could be made at all.

If the regulatory system were effective, the results should be seen in the published material. We did not find this to be so. Articles in journals are not properly reporting the care of animals and the use of post-operative analgesia. Apparently, the major breakdown of this system seems to be at the level of the researcher, between the actual research and the reports. For this reason this study suggests that any changes to be made are best and most easily made in the publication process. Regulations in this area must be stricter and must form a feedback loop with proven regulatory aspects, such as IACUC approval.

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Appendix A: IACUC Protocol Form

Tufts University School of Veterinary Medicine
PROTOCOL FORM (version 6/99)
for review by
Institutional Animal Care and Use Committee
Building #5
200 Westboro Road
North Grafton, MA 01536

For office use only

Protocol #:

Received:

Reviewed:

Approved:

Summary:

All uses of live vertebrate animals must be approved by the TUSVM Institutional Animal Care and Use Committee (IACUC)
Acquisition and housing of all live vertebrate animals must be approved by the office of Teaching & Research Resources (TRR) [formerly the Division of Laboratory Animal Medicine (TRR)].

Instructions

Protocol form must be typed. All sections must be completed. If space provided is inadequate, attach additional sheets. Attaching and referencing a copy of a research proposal cannot be substituted for completing the form. Please contact Dr. Carl A. Kirker-Head at ext. 84827for advice on the Protocol Form completion.

Complete "Agency Notification Request" form (see page 6) if approval letter is needed for a funding agency. Changes limited to project title and/or funding agency can be submitted using additional "Agency Notification Request" forms. Submission of redundant Protocol Forms is unnecessary.

Any proposed changes in animal species, numbers or procedures from those in an approved protocol must be reviewed by the IACUC. Minor amendments can be proposed via memorandum. Major changes necessitate submission of a new Protocol Form.

If project is in collaboration with another institution, a copy of that institution's IACUC approval letter and protocol must be submitted with your completed Protocol Form.

Send completed, signed original Protocol Form to the IACUC, c/o Teaching & Research Resources, Building #5, Grafton Campus. Keep a copy of the Protocol Form for your records. You will receive written notification of the IACUC s review.

A. Project Information

Principal Investigator (must be TUSVM Faculty):

Department/Institution:

Mailing address:

Office Phone : Lab Phone: Home Phone:

Other Personnel Involved:

Lab Phone: Other Phone:

Project Title:

Anticipated Start Date: Duration of Project:

B. Rationale for Animal Use

Describe the **purpose** and **importance** of the proposed animal use **in lay terms**. Address the appropriateness of the numbers and specie of animals to be used.

C. Categorization of Animal Use

	Species A	Species B	Species C	Species
1. **Animal species to be used** (e.g. mouse, dog, rabbit)				
2. Total number to be used per year:				

3. **Source of Animals:**	Species A	Species B	Species C	Species
TRR Vendor:				
Client owned : (consent form must be included)				
Donation:				
Other:				

4. **Projected housing location:** may be completed by TRR: _____

Assessment of animal pain and/or distress

Number of animals used annually
(place **each** animal listed above in a **single** pain category)

	Species A	Species B	Species C	Species
Number of animals to be used in procedures with minimal, momentary or no pain of distress **(USDA Category C):**				
Number of animals that will receive appropriate anesthetics, tranquilizers or analgesics to alleviate pain and/or distress **(USDA Category D):***	*	*	*	
Number of animals that will experience pain and/or distress without alleviation **(USDA Category E):***	*	*	*	

* If research involves any procedures in these categories, Section E on page 3 **must** be completed.

Will the use of animals include the following? (If "yes", a copy of approval letter from appropriate TUSVM Committee must accompany the IACUC Protocol Form).

Yes ____ No ____ Use of **RECOMBINANT DNA** in live animals. If "yes", explain in Section D.

Yes ____ No ____ Use of **RADIOISOTOPES** in live animals. If "yes", attach a copy of **RADIATION SAFETY PROTOCOL** relevant to this project and approved by Health Physics.
Isotopes: _____ Animal
Dose: _____

Yes ____ No ____ Use of **INFECTIOUS AGENTS** in live animals. If "yes", **describe safety precautions** relevant to the project in Section D
Refer to CDC/NIH Guidelines.
Agent: _____ Biosafety Level # Recommended:
_____

Yes ____ No ____ Use of **CARCINOGENS** or other **BIOHAZARDS** in live animals. If "yes" **describe safety precautions** relevant to the prc in Section D.
Agent: _____ Animal Dose:
_____

Yes ____ No ____ **NEOPLASIA** is live animals. If "yes", Consult Committee guidelines and explain procedures in Section D.

Yes ____ No ____ **RESTRAINT** of unanesthetized animal(s) for more than 30 minutes. If "yes" explain in Section D,

Yes ____ No ____ Study of **STRESS, PAIN** or **ALTERED BEHAVIOR** in animals. If "yes" explain in Section D.

Yes ____ No ____ **MORE THAN ONE SURGICAL PROCEDURE** in any animal. If "yes" explain experimental design in Section D.

Yes ____ No ____ Live animals **TRANSPORT** to or **HOUSING** at any site **OTHER THAN TRR ANIMAL FACILITY**. If "yes", contact TRR fo guidelines and complete the following:
Reason for removal of animal(s);
_____
Duration of non-facility housing:

Will live animals be returned to TRR facilities? Yes _____ No _____

D. Experimental Design and Method

Describe **all procedures** which will be performed on live animals within **each** experimental group. Indicate number of animals in each grou Describe how procedures and administered compounds will affect animal health. If surgical procedures are to be performed, Section F mu also be completed.

E. Verification of Lack of Alternative Methods (must be provided for any entries in USDA Categories D or E on page 2)

The Principal Investigator must provide a written narrative of the sources consulted to determine whether or not alternatives exist to procedures which may cause pain or distress. Consideration of alternatives to each procedure which may cause pain or distress must state sources consulted, such as Biological Abstracts, Index Medicus, Medline, the Current Research Information Service (CRIS), and the Anima Welfare Information Center (AWIC). The written narrative should include: the databases searched or other sources consulted, the date of th search and the years covered by the search, the key words and/or search strategy used by the Principal Investigator and the number of references generated when considering alternatives or descriptions of other methods and sources used to determine that no alternatives w available to the painful or distressful procedure. The narrative should be such that the IACUC can readily assess whether the search topics were appropriate and whether the search was sufficiently thorough. Reduction, replacement, and refinement (the three R's) must be addressed, not just animal replacement.

F. Description of Surgical Procedures

__ **Check here if NO SURGERY is performed and go to Section G, on page 5.**

2. **Person(s) responsible for performing surgery:**

Work Phone: _____ Home Phone: _____

3. **Person(s) responsible for post-operative monitoring:**

Work Phone: _____ Home Phone: _____

Type(s) of surgical procedures:

	Number of animals used annually (place **each** surgery recipient in a **single** category)			
	Species A	Species B	Species C	Species D
All surgical procedures will be **terminal**. Animals will be euthanized under anesthesia when procedure is completed.	_____	_____	_____	_____
All surgical procedures are intended to be **non-terminal**. Aseptic surgical techniques will be used.	_____	_____	_____	_____
The experimental plan includes both **non-terminal and terminal** surgical procedures for each animal.	_____	_____	_____	_____

Location where surgery is to be performed (Major survival surgery on non-rodents must be performed in a dedicated operating room):

5. **Agents administered:** **Agent name, dose, route and frequency:**

Pre-anesthetic agent(s): _____

Anesthetic agent(s): _____

Inter-operative agent(s): _____

Post-operative agent(s): _____

NOTE: "As needed" **is not appropriate for frequency.**

Description of surgical procedure(s):

G. Post-Procedural Care of Animals (Post-operative care records must be maintained for all non-rodent surgical cases)

Describe the care of animals following **surgery** and/or **other procedures** (e.g. tumor or infectious agent inoculation, drug administration, carcinogen exposure, etc.) that may affect animal health. Include the **names and dosages of antibiotics and analgesics** to be administered. Specify the **frequency and method of animal monitoring** to be provided by the research staff. Indicate how the need for treatment or euthanasia of animals will be determined and who will be responsible for that determination.

H. Disposition of Animals Following Study

Yes _____ No _____

All animals described in this protocol **will be euthanized** upon completion of this experimentation. If "no", describe the fate of animal(s). (Please note that no animal may be given away without permission from IACUC).

NOTE: Transfer/adoption form and any other appropriate forms must be submitted to TRR prior to animal disposition.

All protocols (regardless of answer to above question) **must include euthanasia plan** for each animal species in case euthanasia becomes necessary.

Method(s) of euthanasia:
(Agent name, dose and route if applicable) _____

Individual(s) responsible for administering euthanasia: _____

What tissues from euthanized animal(s) will be available for utilization by other investigators?

Investigator's Statement

The information I have supplied above is a complete and accurate description of all procedures involving live animals in this project. I have taken appropriate measures to ensure that I an using the minimum number of animals to achieve my goal and that I am not unnecessarily duplicating known results.

I assure that all personnel under my direction will be appropriately trained prior to handling animals. I agree to abide by the animal care and use policies of this institution.

_____ _____

Signature of Principal Investigator Date

Tufts University/School of Veterinary Medicine

Institutional Animal Care and Use Committee

Agency Notification Request

For office use only

Protocol #:

Received:

Approved:

Summary:

Instructions

1. Complete this form only if you need an approval letter sent to a funding agency. Agency Notification Request(s) can accompany or follow Protocol Form submission. Request(s) will not be processed until the associated Protocol Form has received Institutional Animal Care and Use Committee approval.

2. One approved Protocol Form can be used for the generation of approval notifications to several potential funding agencies. The Protocol Form must contain all animal species, numbers, and procedures relevant to any associated grant application.

3. Send completed, signed Agency Notification Request(s) to the Institutional Animal Care and Use Committee, c/o DLAM, Building #5, Grafton Campus. The Committee will send notification of animal procedure approval directly to the agency unless otherwise instructed by the investigator. A copy will be sent to the investigator. Please call 839-7992 if you have any questions about funding agency notification.

A. Protocol Form pertaining to this Request is: (choose one only)

_____ Attached

_____ Protocol Form #_____

B. Provide funding agency information to be included in letter or agency form:

Funding agency office/contact person and address (be as specific as possible):

Agency Fax Number (if known):

Title of project as listed on grant application:

Grant application number (if known):

Vertebrate animal species to be used in this project:

Principal investigator(s) for this project:

Investigator's institution:

C. Investigator's Statement

I certify that all animal species, numbers, and procedures proposed in the project named above have been completely described on the associated Protocol Form. Any proposed changes in animal species, numbers, or procedures will be submitted in writing to the Institutional Animal Care and Use Committee.

_____ _____

Signature of Principal Investigator Date

Appendix B: The Problem With Assessing Pain

There are two prevailing methods of pain assessment in animals, subjective and objective. A subjective assessment includes a visual appraisal of the animal. The visual impressions and consequent judgment of the assessor determines any need for analgesia. For example, an animal that is vocalizing in a certain way; seems to be agonizing or lethargic; or refuses to participate in normal activity such as the consumption of food or the act of bearing its own weight may be considered to be a painful animal. However, there is no standard here. Post-operative animals may potentially be checked more often or less often than needed. The personnel observing the animal may judge its behavior incorrectly. There is nothing concrete to assure adequate and correct assessment.

An objective assessment is performed using an instrument expressly for this purpose, for example, an algometer. This instrument is applied externally to the limb or affected site involved in the experiment. Pressure from the assessor is applied to the device, and the amount of pressure exerted before the animal responds is noted. This measurement is used to determine the level of discomfort in the animal and discern whether the treatment is effective, however this is not used to assess pain in a clinical setting. Other graded assessment schemes exist using heat, electrical current or a pinprick in a similar manner.

Still, there is an additional possibility for error. Even if either method of pain assessment is performed in an ideal manner, proper treatment is still not assured. The analgesics used to treat laboratory animals are not standardized in any way, because pain can vary due to surgery technique and species/individual. Although guidelines regarding appropriate dosages exist, they may not be widely known.

Many times pain medication is administered "as needed." This means that animals are checked on set schedule and only when they exhibit signs of pain do they receive the proper analgesics. This is an suboptimal manner of treatment for many reasons. First, as previously stated, there is no standard for pain assessment, therefore the need for analgesics cannot be accurately determined. Another reason is that many animals so not display that they are in pain, they appear to be normal, all the while hiding their discomfort. Because of this, animals may be in pain but not receiving the proper treatment because their distress has gone unnoticed. The most important reason why analgesia "as needed" is inappropriate is due to the elapsed time between checks. Many times if no routine procedure is occurring, the animal is not checked often. It is possible for an animal not to be in pain at the moment of the observation, however develop pain in the next few hours. Because the next check is not for many hours this animal must sit in pain. If a set schedule of pain medication is set out, even if the animal is not in obvious pain when the next dosage is given it assures that they will not be in pain until the next set time. Also animals not showing signs of pain will be treated regardless of their visible appearance

Appendix C: Anesthesia and Analgesia Response

S.F. Office Review
ANESTHESIA & ANALGESIA
Manuscript Review-Editorial Office Copy (Confidential)

Editorial Office: 5 Third Street, Suite 1216
San Francisco, CA 94103
Phone: 415/777-2750
Fax: 415/777-2803

Editors/Consultants: Within three weeks, please fax this Manuscript Review Form and the Reviewer's Comments Sheet(s) with your comments to the San Francisco office OR to the Control Reviewer. Please destroy the manuscript, but return any glossies. (Be sure to identify them by manuscript number.)

Manuscript Number:

Reviewer: **Consultant:**

Corresponding Author:

Title of Paper:

Mailed From Editorial Office: **Return by:**

Returned by Reviewer:

Scientific Validity Excellent ___ Adequate ___ Inadequate ___

Significance/Importance Considerable ___ Modest ___ Negligible ___

Interest to our readers Considerable ___ Modest ___ Negligible ___

Originality Yes ___ No ___

Presentation Good ___ Adequate ___ Inadequate ___

Publishable Accept as is ___ Adequate with some revision ___

Possible accept after major revision/rewrite___ Reject ___

Statistical consultation needed ___

Disclosure of Possible Reviewer Conflict

___I have a financial conflict (e.g. stock ownership in sponsoring company or competitor, etc.

___I have received funding from the sponsoring company within the last five years.

___I have reviewed this MS for another journal.

___I view myself as an "academic competitor" of the author.

General Comments (for Editorial Office Only)

A Guide for Authors

Manuscripts should be sent to:

Ronald D. Miller, MD
Editor-in-Chief
Anesthesia & Analgesia
The Hearst Building
5 Third Street, Suite 1216
San Francisco, CA 94103
Editorial Office E-Mail Address: sleepers@lmi.net
Anesthesia & Analgesia Web site: http://www.anesthesia-analgesia.org/

Editorial Policies

Anesthesia & Analgesia, the oldest publication for the specialty of anesthesiology, is the official voice of the International Anesthesia Research Society, the Society of Cardiovascular Anesthesiologists, the Society for Pediatric Anesthesia, and the Society for Ambulatory Anesthesia. It publishes general articles, case reports, brief reports, technical communications, review articles, special articles, medical intelligence articles, editorials, book reviews, and letters to the editor. Articles will, when possible, be assigned to one of the subspecialty sections (Ambulatory Anesthesia, Cardiovascular Anesthesia, Critical Care and Trauma, Economics and Health Systems Research, Neurosurgical Anesthesia, Obstetric Anesthesia, Pediatric Anesthesia, and Regional Anesthesia and Pain Management). All papers are reviewed by three or more referees. Acceptance is based on significance, originality, and validity of the material presented.

Duplicate Publication

The submitted manuscript should be accompanied by a cover letter stating that neither the manuscript nor any significant part of it is under consideration for publicaton elsewhere, or has appeared elsewhere in a manner that could be construed as a prior or duplicate publication of the same, or very similar, work. Should there be a possibility of doubt concerning such prior publications, the title page and abstract of such material should be included with the submitted manuscript. When appropriate, the cover letter should contain disclosures of any potential conflicts of interest arising from associations with commercial or corporate interests in connection with the work submitted. *The cover letter must be signed by all authors and must list a word count for the manuscript* (see word limitations listed in "General Information"). Manuscripts must be prepared and submitted in the manner described in "Uniform Requirements for Manuscripts Submitted to Biomedical Journals," reprinted in *The New England Journal of Medicine* 1991;324:424-8.

Human Subjects

No manuscripts describing investigations carried out in humans will be accepted for publication unless the text states that the study was approved by the authors' institutional human investigation committee and that written informed consent was obtained from all subjects or, in the case of minors, from parents. Human subjects should not be identifiable. Do not use patients' names, initials, or hospital numbers.

Animal Subjects

No manuscript describing investigations in animals will be accepted for publication unless the text states that the study was approved by the authors' institutional animal investigation committee.

Authorship and Copyright

The manuscript cover letter must stipulate that all persons listed as authors have contributed to preparing the manuscript, and that no person or persons other than the authors listed have contributed significantly to its preparation. The intent of this requirement is to forestall the participation of outside parties ("ghost writers") who may stand to benefit by attempting to influence the content of a study or its results. Authors will be asked to transfer copyright of articles accepted for publication to the International Anesthesia Research Society.

Authors and their typists should use the checklist given below for preparation of manuscripts.

General Information

- ☐ General articles describe clinical or laboratory investigations.
- ☐ Case reports describe either new and instructive cases, anesthetic techniques and equipment of demonstrable originality, usefulness, and safety, or new information on diseases of importance to anesthesia.
- ☐ Brief reports describe clinical or laboratory investigations that do not require the breadth of experimentation or support required by a general investigative article.
- ☐ Technical communications describe instrumentation and analytic techniques.
- ☐ Review articles collate, describe, and evaluate previously published material to aid in evaluating new concepts.
- ☐ Medical intelligence articles usually collate, describe, and evaluate previously published material to aid in evaluating new concepts or updating old concepts or topics germane to anesthesiology.
- ☐ Special articles describe literature, education, societies, and other topical interests of a historical or current trend in anesthesiology.
- ☐ Editorials (solicited by the Editorial Board) comment on articles published in the journal and/or express the general policies or opinions of the Editor-in-Chief.
- ☐ Book and multimedia reviews report current literature in anesthesiology. Please send all books and multimedia for review directly to Norig Ellison, MD, Book Review Editor, Department of Anesthesia, University of Pennsylvania, Philadelphia, PA 19104.
- ☐ Letters to the editor include brief constructive comments concerning previously published articles or brief notations of general interest. The manuscripts must be double-spaced, and a title and three copies must be provided. **Letters may be submitted online at lettered@lmi.net. Letters submitted electronically must include the author's mailing address as well as an e-mail address.**
- ☐ When submitting your manuscript, please observe the maximum word count allowed for each type of submission and the maximum allowance for figures, tables, and references (word count should reflect text only and must be listed in the cover letter):

Maximum Word Allowances	
General Article	3000 words (excluding abstract)
Case Report	800 words
Brief Report	1000 words
Technical Communication	1500 words
Review Article	4000 words
Medical Intelligence Article	3000 words
Special Article	2000 words
Editorial	1500 words
Book Review	750 words
Letter to the Editor	200 words
Abstract	200 words
Implications	50 words

Nontextual Material	Maximum Allowance
Figures and Tables	No more than 3 each or a combination of 6 total. Do not duplicate data in the tables and figures.
References	No more than 25 references per article. For a review article, up to 40 references are acceptable.

- ☐ For *all* general articles, case reports, brief reports, and technical communications, even when intended for a subspecialty audience, authors must provide a 25- to 50-word description, *in language understandable to the lay reader* (i.e., a reader who has some understanding of scientific method), of why their study is important and how it was performed. This statement should be appended to the Abstract after the heading "Implications."

Manuscript Preparation

- ☐ Type manuscripts using double- or triple-spacing (to allow room for editing) throughout, including references and table and figure legends.
- ☐ Begin each of the following sections on separate pages; title page, abstract and key words, text, acknowledgments, references, tables (each table, complete with title and footnotes, should be on a separate page), and legends. Number pages consecutively, beginning with the title page.
- ☐ Submit one original plus three copies of the manuscript and four sets of figures. Submitted manuscripts should be accompanied by the cover letter, which includes a manuscript word count, and by letters granting permission to reproduce previously published materials or to use illustrations that may identify subjects.
- ☐ When appropriate, authors should specify the subspecialty section for which their submission is intended (e.g., Cardiovascular, Ambulatory, Critical Care, etc.).
- ☐ Authors should keep copies of everything submitted and all correspondence from the editorial office and its board members.
- ☐ Authors should not submit computer disks with the original manuscript to the editorial office.

Title Page

- ☐ The title page should contain the title of the article, which should be concise but informative;
- ☐ A short running head of no more than 40 characters (count letters and spaces) placed at the bottom of the title page and identified;
- ☐ First name, middle initial, and last name of each author, with highest academic degree(s) including fellowship and board affiliations; each listed author must (a) have participated in the work to the extent that he or she could publicly defend its contents; (b) have read the manuscript before its

Appendix D: American Journal of Veterinary Research Response

AMERICAN VETERINARY MEDICAL ASSOCIATION
1931 N. MEACHAM ROAD, SUITE 100 • SCHAUMBURG, ILLINOIS 60173-4360
PHONE 847-925-8070 FAX 847-925-1329

April 10, 2001

Joan Norton
Lauren Barker
Worcester Polytechnic Institute
100 Institute Road, Box #924
Worcester, MA 01609

Dear Ms Norton and Barker,

Thank you for your interest in the AVMA journals. I have enclosed a copy of our guidelines for reviewers of manuscripts submitted for publication in the *Journal of the American Veterinary Medical Association*; guidelines for reviewers of manuscripts submitted for publication in the *American Journal of Veterinary Research* are exactly the same. We do not have any page limits for these journals, nor do we have strict limits on the length of individual articles published in the journals.

I have also enclosed a copy of an editorial we published in 1996 on the responsible use of research animals. As stated in the editorial, we believe that a statement that the authors' experimental protocol was approved by an institutional animal care and use committee provides some reassurances that animals were treated humanely. However, such a statement does not, in and of itself, provide sufficient information about the care experimental animals received and is not a substitute for a full description of the care of the animals used in the study. For this reason, we do not specifically require that authors indicate whether their experimental protocol was approved by an institution animal care and use committee.

I hope that this information is of some benefit to you. If you have additional questions, please do not hesitate to contact me.

Sincerely,

Kurt J. Matushek, DVM, MS
Associate Editor

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Guidelines for reviewers of manuscripts submitted for publication in the *Journal of the American Veterinary Medical Association*

Authors submit their manuscripts to the *Journal of the American Veterinary Medical Association* with the understanding that the manuscripts and their contents will be kept confidential until they are published. Manuscripts are the intellectual property of the authors. Therefore, we ask that reviewers not make copies of any manuscript submitted to them for review and that they not discuss the content of any such manuscript with colleagues, students, or other parties. Because the peer review process depends on objective evaluation of manuscripts, reviewers should immediately notify the editor assigned to the manuscript of any personal, professional, or financial conflicts of interest they may have regarding a manuscript or its authors. Although such conflicts do not necessarily disqualify a reviewer, they should be considered when the editor makes a decision about a manuscript's disposition. Reviewers should also contact the editor immediately if they lack the expertise to adequately assess manuscripts submitted to them or if they need opinions from additional experts. Reviewers should not contact the authors directly.

Reviewers should provide fair, objective, thorough, and constructive reviews. Reviewers= recommendations should be based on fact and logic, and reviewers should document and justify their criticisms. Because the review process is a large component in the lag time between submission and publication of a manuscript, reviewers should return their reviews within two weeks.

With all manuscripts sent for review, we include a checklist for reviewers to complete and return. This checklist is not sent to the authors; therefore, we ask that reviewers also include a separate, unsigned critique of the manuscript. This critique should contain a brief overview of the manuscript and comments about each of the manuscript's sections and should clearly identify (by indicating page and paragraph or line number) aspects of the manuscript that were considered marginal or unacceptable. Reviewers should not, in this written critique, comment about whether the manuscript should be accepted or rejected. If a reviewer wishes to comment on how a manuscript that is currently considered unacceptable could be made acceptable, this should be done in a separate note addressed to the editor. **We ask that reviewers not write on the manuscripts themselves, because review copies of the manuscripts are not returned to the authors.**

On the next page, we have included a list of the important indicators of the quality of a manuscript. We ask that reviewers consider these factors when evaluating manuscripts. In general, reviewers should not advise authors to perform more work unless this involves only further analysis of the available data. If a reviewer believes additional studies are necessary before the manuscript could be considered acceptable, the reviewer should recommend rejection of the manuscript. Reviewers should review the manuscript the authors wrote, not the manuscript they believe the authors should have written.

Any questions about these guidelines or about any manuscript that has been submitted for review should be directed to the editor assigned to the manuscript.

5/18/00

Factors To Consider When Evaluating Original Studies

Overview

Importance

- Is the purpose of the study clear and is the objective of the study relevant?
- Are there sufficient new and important findings to warrant publication?
- Has any or all of the information in the manuscript been published previously?

Experimental methods

- Are experimental methods appropriate for the study?

Interpretation

- Do the data support the conclusions?

Presentation

- Is the writing clear, concise, and readable?
- Should any sections of the manuscript be expanded, condensed, or eliminated?
- Have authors used abbreviations or jargon to excess?

Specific Manuscript Sections

Title

- Is the title a clear, accurate representation of the article=s content?

Abstract

- Is the abstract a clear, concise (< 250 words), accurate representation of the major findings of the study?

Introduction

- Is the introduction focused on relevant aspects of the topic, and not just a literature review?
- Is the reason for performing the study clearly stated?

Materials and Methods

- Is the study design valid and are experimental methods appropriate?
- Are experimental methods described in sufficient detail?
- Are methods for selecting test and control subjects appropriate?
- Is there any doubt that animals were treated humanely?
- Do authors address potential confounders and biases in subject selection?
- Are statistical methods valid?

Results

- Are data presented in a clear and understandable manner?
- Do authors account for all animals?
- Are the results credible?
- Are calculations correct (please scan and spot check)?
- Do tables, text, and figures agree with and complement each other?
- Are all tables and figures necessary or is there repetition of material?
- Is the figure quality adequate?

Discussion

- Are any results mentioned for the first time in the discussion?
- Do the authors interpret the data, not just restate results?
- Are strengths and weaknesses of the methods used acknowledged?
- Are any ideas or conclusions over- or underemphasized?
- Do the authors provide a balanced view of the importance of the results?
- Do the authors cite relevant work of others?
- Are all conclusions supported by the results?
- Are any key issues not addressed?
- Is all of the discussion relevant?
- Do the authors make any recommendations not supported by their data or beyond the scope of the study?

References

- Are citations and quotations correct (please scan and spot check)?
- Are all references pertinent, or are some inconsequential?
- Have any important references been omitted (please provide citations)?