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ABSTRACT Institutional Animal Ethics Committees (AECs) are the principal means of ensuring the ethical use of animals in science in many countries, yet we understand very little about how they make decisions and how effective they are in implementing policy and achieving their stated aims. To answer these questions, an ethnographic study involving participant observation and in-depth interviews with 28 members of four university AECs in western Canada was carried out. The major focus of protocol review by committee members was reducing harm to animals, with less focus on the ethical justification of research despite this being stressed in policy as a goal of AECs. In part, this may be due to confusion over the relation between AEC review and scientific peer review by granting agencies, with some members believing that ethical justification is decided by scientific peer review. Members were also unclear on the distinction between the different elements that go into decisions about ethical justification. Use of harm-benefit assessment, although prescribed by policy, did not cover the various other decision-making approaches that members described using (moral intuition, empathy with animals etc.). Thus, policy may invalidate how some (especially non-scientist) members naturally make decisions. AEC effectiveness could be improved by clarifying the elements of harm-benefit assessments and the relation between AEC and scientific peer review, keeping in mind that peer review does not offer the same assurances (notably community input) that the AEC brings. Effectiveness could be improved by expanding policy to acknowledge the various approaches used in decision-making.

Keywords: animal ethics committees, decision-making, ethics review, harm-benefit analysis, interviews

Institutional Animal Ethics Committees (AECs)—the equivalent of the Animal Care Committee in Canada, Institutional Animal Care and Use Committee in the USA, Animal Experimentation

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Ethics Committee in Australia, and Ethical Review Process in the UK—are the principal means of ensuring the ethical use of animals in research, teaching, and testing in many countries. Although mandates may vary, in general they all include the aim of protecting research subjects via substantive, structural, and procedural standards. They have the responsibility of ensuring humane care and use of animals by reviewing proposals to use animals and by educating animal users in their institutions. The task of the AEC is a challenging one, requiring an understanding of complex and contentious concepts such as pain and distress in animals, and a technical understanding of scientific procedures and animal care practices. Understanding how these diverse groups of people make decisions about the care and use of animals is a key step in ensuring that this system functions effectively.

Regulatory contexts differ. For example, in Canada institutional committees approve, modify, or reject each proposal, whereas in some countries committees have only an advisory role, with final approval resting with a statutory body such as the UK Home Office. The AEC in Canada is similar in composition to comparable committees in other countries and usually includes a selection of members drawn from within the institution: scientists and/or teachers experienced in animal care and use, veterinarians, non-animal-users, and animal technical staff, together with people independent of the institution and representing community interests. The relative proportion of each type of member varies between countries. For example, committees in Canada must have at least one scientist, one veterinarian, and one community member (CCAC 2006). Committees in Sweden have an equal number of community members and scientists or members who work with laboratory animals (European Biomedical Research Association 1979).

In general, AECs make decisions at two levels: firstly, they must ensure that the proposed research is justified, and secondly they must decide what modifications are required to minimize harm to animals. In many countries (CCAC 1997; FELASA 2007) policy requires that AECs make decisions using a harm-benefit assessment. Typically this involves weighing the potential benefits to humans or animals against the harms to the animals used in research. In general, the higher the level of anticipated harm, the stronger must be the justification of the value of the research. Beyond this weighing of harm and benefit, certain ethical limits may also be identified. Canadian policy requires that committees should carry out a "cost/benefit assessment which involves consideration of relevant ethical, scientific, and social issues" and "the intensity of the review should vary directly with the level of invasiveness of the procedures." Costs "must be measured against the expectation of a proportional contribution to the understanding of fundamental biological principles, or to improvement of human or animal health and welfare" (CCAC 1997). In general, harms include pain and stress from experimental procedures, and reduced comfort or well-being resulting from inappropriate housing, care, and handling.

To aid members in identifying ways to minimize harms, AEC decisions are guided by the "Three Rs" (Russell and Burch 1959)—Replacement, Reduction, and Refinement—which are widely recognized principles for minimizing harms to animals. In addition, various systems for categorizing the degree of pain or suffering experienced by animals have been created. These tend to focus on the duration and frequency of a procedure. The Canadian Council on Animal Care (CCAC) has adopted a scale of "Categories of Invasiveness in Animal Experiments," ranging from experiments that cause little or no discomfort or stress (B), to experiments that cause minor stress or pain of short duration (C), to procedures which cause severe pain (E) (CCAC 1993).

Decisions during the review of proposals are likely influenced by policy and guidelines, institutional culture and by the views, values, and decision-making processes of individual members. Aspects of committee structure and process—committee composition, deliberation process, group dynamics, and training—can also affect decisions (Schuppli and Fraser 2007).

Various frameworks based on harm-benefit assessments have been developed to aid members to make orderly and systematic decisions about the ethical acceptability of experiments (Smith and Boyd 1991; Porter 1992; de Cock Buning and Theune 1994; Mellor and Reid 1994; Stafleu et al. 1999; APC 2003). Ideally these frameworks should help to increase consistency in decision-making, although their effectiveness has not yet been tested. However, decision makers in natural settings rarely use such analytical approaches which involve reasoning, weighing of evidence, and selecting an optimal course of action (Klein 1998; Slovic 2006). Indeed, affect has been shown to play an important role in decision-making (Slovic 2006), as well as intuition (recognizing familiar patterns based on experience) and mental simulation (imagining how a decision would play out) (Klein 1998). Galvin and Herzog (1992) found that students acting as AEC members sometimes used different paths of reasoning to arrive at the same decision, and sometimes used similar reasoning to arrive at different decisions.

In order to evaluate the functioning of AECs, we need to understand how individual AEC members make decisions in their natural setting. Three studies surveyed actual committee members. They examined consistency of decision-making across institutions (Dresser 1989; Plous and Herzog 2001) and within committees (Plous and Herzog 2001), and how member's ethical views influenced their understanding of the harm-benefit assessment (Ideland 2009). Stafleu, Heeger and Beynen (1989) and Stafleu et al. (1993) examined to what extent harm-benefit assessments are used by scientists, veterinarians, animal technicians, but not specifically AEC members. Galvin and Herzog (1992) surveyed undergraduate psychology students acting as hypothetical committee members. Most of these studies rated the importance of several factors (preselected by the researcher) to decision making. Only two studies specifically attempted to characterize individual decision-making processes by analyzing written responses to an open-ended question (Galvin and Herzog 1992) or interviewing members (Ideland 2009).

The present study used an ethnographic approach to explore how AEC members in Canada make decisions about proposed research in practice. In-depth interviews were carried out with individual AEC members to examine to what extent harm-benefit assessments are used to make decisions about the justification of research and about necessary modifications, what other decision-making approaches are used, and what factors influence decisions. These interviews were also used for two additional analyses: 1) to examine whether AEC members interpreted the Three Rs appropriately and consistently or focused on a particular "R" more than others, and whether the Three Rs functioned as effective mnemonic tools in proposal reviews (Schuppli and Fraser 2005) and 2) to identify structural and procedural factors (committee composition and dynamics, member recruitment, motivation for joining, workload and participation levels) that may influence the effectiveness of the protocol review process (Schuppli and Fraser 2007). In all cases, the results were used to identify gaps between policy and practice, to identify places where policy may be insufficient for effective AEC functioning, to highlight challenges faced by AEC members and committees as a whole in achieving their mandate to protect animal subjects, and to suggest ways for improvement.

Methods

Data collection included both participant observation and interviews. While serving as student representative on the AEC at University A, I was a participant observer for 2.5 years where I attended 26 meetings, reviewed and evaluated 587 protocols, and attended 26 animal facility inspections. For complete details on methods, see Schuppli and Fraser (2005).

Twenty-eight members of AECs at four universities in western Canada were interviewed during 2001 to 2002. Committees and interview participants were selected by purposive sampling to represent variation in the amount and type of research reviewed. Committees ranged from 9 to 17 members, and averaged 13 to 311 protocols (term used by participants for proposals) per year in a mixture of biomedical, wildlife, agricultural, veterinary, and biological research, plus product testing and teaching. Protocol application forms varied per university but all required information about the project objectives and value of the research, names and training of personnel working with and caring for animals, funding sources, length of project, number of animals and species and why that number was needed, where they were located, whether Replacement had been considered, and a detailed description of procedures, end points of study, euthanasia technique and expected morbidity mortality rates, and criteria for euthanasia or Refinement. All the committees reviewed protocols ranging from little or no discomfort or stress to moderate or severe discomfort or distress (categories B–D on the scale of the CCAC [CCAC 1993]), and three universities had reviewed more than one protocol of severe pain, near or above the pain tolerance threshold (category E) during 1999 to 2001. Most protocols had been peer reviewed by granting agencies before submission to the AEC. The veterinarians and the AEC carried out post-approval monitoring and the AEC received annual reports from researchers. Note that in Canada research carried out in universities must receive AEC review in order to receive research funding (CCAC 1993).

Participants included six community representatives (4 females, 2 males), 13 university scientists experienced in animal research (2 females, 11 males), four university animal care technicians (2 females, 2 males), three university veterinarians (2 females, 1 male), and two university non-animal-users (1 female, 1 male).

Interviews were semi-structured and lasted 1 to 2.25 hours at locations chosen by participants. Interviews were tape-recorded and transcribed verbatim. To gain an accurate reflection of participants' perspectives and behaviors, questions were open-ended, and allowed members time to reflect and elaborate on or add points they considered important. As a result, the interviews varied in their content and direction as the researcher probed the participant on topics raised by the researcher and topics raised by the participant.

Interview questions covered two major themes: evaluation of protocols (presented here) and committee process (Schuppli and Fraser 2007). Interviews began with factual questions about committee processes and the participant's role on the committee. All members were then invited to talk about how they reviewed and evaluated protocols. They were all asked to "walk me through the process of how you would go about reviewing a protocol": what modifications they would request, what protocols they found challenging to review and evaluate, how they decided in these cases, whether they used any guiding principles for making decisions, the role of species of research animal in decisions, the role of AECs in judging scientific merit, and personal attitudes and ethics regarding animal use in research. All participants were invited to talk about their understanding and use of the Three Rs (Schuppli and Fraser 2005). To document institutional variations in AEC decision-making, I observed one committee meeting at each university.

Transcript data were analyzed using an established system of coding (LeCompte and Schensul 1999) to identify themes relevant to understanding the issues, values, concerns, behaviors, and responsibilities, as expressed by AEC members. Attention was paid to commonality as well as differences among comments between members. Themes were developed based on responses to particular questions as well as inductively from the entire data. Upon completion of analysis, results were sent to participants for comment. A range of quotes are presented in the results to illustrate the themes identified and to demonstrate the coding approach of the author.

Analysis for this paper focused on 1) how individual participants evaluated protocols and 2) what factors influenced their decisions. Attention was also paid to similarities and differences in the expressed views of different types of committee members. Although the approach was qualitative rather than quantitative, the number of members expressing certain views is reported, in order to give the reader a sense of their prevalence. The numbers need to be interpreted with caution because although all participants were asked the same set of questions, participants were encouraged to raise points that they felt were relevant, thus conversations varied. It is important to note that views expressed by participants are their accounts of their decision-making, not necessarily how they made decisions in practice or how decisions were made by the AEC as a whole.

The Behavioural Research Ethics Board at University A approved the study. Pseudonyms for participants and universities were used in field notes and transcripts, and all participants gave informed consent. In this paper, participants are identified with codes beginning with letters representing their group (C, community member; N, non-animal user; S, scientist; T, technician; V, veterinarian) followed by a number.

Results

Factors that Influenced Decisions

When members were asked how they evaluated protocols, most members did not have a well articulated description of their decision-making process. Rather, they typically gave a procedural description that revolved around the content of the application form.

Harm-Benefit Assessment: Half of the members specified that they tried to use a form of harm-benefit assessment to evaluate justification of proposed research. However, this assessment varied and members found it challenging. Some (7) required evidence that benefits outweighed harm caused to animals; others (2) accepted evidence of some potential benefit to people regardless of harm caused to animals; and in some cases (5) justification was considered to be important only in those extreme cases where costs were perceived to be extremely high or benefits were perceived to be very low (5).

For example, V1 suggested that her committee would defer a protocol where it, "didn't seem that the benefits of doing this work outweighed the costs to the animals it was going to entail." V3 justified vaccine research because it would benefit a greater number of animals than it would harm: "… That's how I'll justify challenging ten pigs, because I might save discomfort in ten thousand pigs."

Members also identified several shortcomings to the use of a harm-benefit assessment. Firstly, seven members felt that there were certain limits to acceptable levels of suffering to animals, regardless of benefits of the research. T4 recounted that, "The invasiveness had to be within an acceptable range ... You may have a miracle drug but if the invasiveness is off the

scale, then it's still not justified for the animal." V2 believed that no research should be permitted if it fell into Category of Invasiveness E (the highest level of invasiveness in the system of the CCAC 1993). C3 felt the same about LD50 experiments (to determine the dose of toxin which kills 50% of exposed animals). V1 would not approve a burn study. S8 considered that procedures that produced "very debilitated, sickly, moribund animals" should be limited. T3 struggled with weighing harms against benefits because she found it difficult to decide what was an acceptable amount of suffering (where to "draw the line"), especially for important health research: "I think sometimes it's very difficult because you can see the value but ultimately the animal's still suffering ... if it's life-threatening in humans and you want to, you know, make a change, how far do you go?"

T3 also described how weighing of potential benefits against harms might not be a suitable approach for lay members (representing public concerns) because they may consider some procedures unacceptable based on moral intuition and not a rational calculus: "To a lay person those [harm-benefit assessments] are ... not concrete things and I would think there are some things that ... they just think, "Why would you ever do that?" There's no way that there is any kind of cost-benefit … and I think they should be allowed to express that because really that's what the public would express."

Secondly, five members felt that harm-benefit analysis may be impossible to use because benefits may be too difficult to assess. S9 pointed out that his committee mostly focused on harms because of the difficulties of predicting potential benefits: "Benefits of science are totally unpredictable. It is often 50 years later when we can actually benefit. So ... making decisions about benefits is difficult. I think it is mostly cost that we look at."

Thirdly, two members implied that they rarely involved harm-benefit analysis because they felt that any benefit justified an experiment, as long as the researchers complied with policy. As C1 put it: "Obviously I completely believe in animal research or I wouldn't be on the committee. So if anybody is going to come up with some good, no matter how minuscule it is, out of any one of those proposals, then I think it's justified."

Finally, members differed in what they considered benefits. For example, members often described benefits from health research as worthwhile, but four members felt that cosmetic development or testing did not generate benefits that would justify the use of animals.

Role of Peer Review: Participants often seemed to conflate peer review, scientific merit, social value, and the justification of research. For clarity of presenting results, I define these terms as follows. Scientific merit (the terminology often used by participants) is the value of the work as a contribution to science and includes scientific relevance, quality of the experimental design, appropriateness of animal model and procedures, and skill of the researcher. Social value is the ability of the work to make a positive contribution to society. Justification of the research refers to a rationale for the work to proceed; this might involve weighing the scientific merit and social value against harms to animals. Two patterns emerged about how peer review by granting agencies or experts affected decisions. First, 13 members took peer review as an assurance of scientific merit but they varied in their definition of scientific merit (often including scientific merit, social value, and the justification of research). Eleven members were hesitant to critique peer review because they believed that it was not the responsibility of AEC or because they were not qualified to assess scientific merit. Two scientists described this view: "I don't get stuck up in the science because that's supposed to be done by somebody else" (S8) and "I don't think that we [AEC] should be trying to take on the role of being scientific reviewers

because the expertise is not there on the committee and never will be, can't be. You really need the experts in the field to evaluate the scientific value of something" (S7).

In contrast, S12 expressed the less common view that the scientific merit should be evaluated; in fact, it was his major focus in reviewing protocols: "To me the major issue is quality of science. So whenever I review a protocol that is the one thing I am constantly trying to evaluate: is this good science?" However, S12 also added that his committee may not have the power to give a negative recommendation for an application if it had been approved for funding.

Second, the majority of members (23) seemed to take a stronger position that approval by peer review was an assurance not only of scientific merit but also of social value and that the research was justified to proceed. Thus, the role of the committee was mainly to focus on minimizing harm to animals. Nine members who reported using a harm-benefit assessment remarked that they accepted approval of a protocol by a peer-review committee as justification for the study to proceed, without further weighing of harms and benefits. For example, S3's view was that, "If the research is supported by peer-reviewed grants, I don't concern myself too much with the purpose of the study. I am more concerned with, is the study going to involve any pain for the animal?" Asked whether he would challenge the peer review process, a veterinarian (V3) answered, "I probably won't question the research so much as I'll question, you know, why do they need this number of animals, why does this animal appear to be the model that they've chosen."

Although participants generally demonstrated a high level of trust in peer review, 11 believed that AECs should reserve the right to question the quality of any peer review, in part because they lacked confidence in the peer review process. C3 pointed out the danger of relying entirely on peer review. He suggested that because peer review only assesses one part of the harm-benefit assessment (namely, the scientific merit), AECs need additional elements to decide whether research is justified: "I wonder how concerned they [granting agencies] are with anything other than the strict scientific merit. I wouldn't think so. The question of value for pain … is not considered at that level. And if the AEC is not going to use that judgment, then nobody is going to." S9 also pointed out that where granting agencies fund overall programs rather than individual experiments, peer review may not evaluate each experiment in an application. As a result of concerns about inadequate peer review, a few members indicated that they would be more likely to scrutinize the justification of studies with higher levels of invasiveness.

Attention to Animal: Eight members focused their protocol review on trying to understand what is happening to the individual animal throughout handling and experimental procedures. S7 considered this so important that she saw other issues as distractions and tried "to stay focused on the animal." T3 put her approach in these terms: "I tend to be looking at the protocol more from the animal aspect and I'm trying to understand what's happening to the individual animal—not really thinking of the scientific design and those sorts of things."

A focus on the animal occasionally involved a process of projection. Two members reviewed protocols by imagining themselves as the animal subjects. For example, a guiding principle of T2 was, "putting yourself in the position of the animal." V2 used projection to assess the level of harm to animals, which she then balanced against benefits. Other participants reported projecting onto animals what humans would experience. For example, V1 described the difficulties of pain management: "You see what people go through, and even with the best drugs that exist you still might not be able to maintain the pain-free status." In contrast, S8 suggested that it was "arrogant" of humans to believe they could understand an animal's

viewpoint and that there is a danger of AEC members, "assuming what the animal feels." In a slightly different manner, T2 used projection to imagine herself as the technician or researcher who would be carrying out the proposed procedures and asked herself, "Can I do this myself? Would I feel comfortable doing this myself? ... Could I psychologically do this to an animal and not feel bad about what I was doing?"

Emotion and Moral Intuition: Emotive language was used primarily by community members and technicians to describe both their approach to decision-making and their general reactions to reviewing protocols and to specific procedures. Two community members described their approach to protocol review as "gut feel" rather than a well-thought-out logical or systematic judgment, such as harm-benefit assessments. C2 described her approach as a "smell test" that involved intuitive judgments such as, "This doesn't sound right to me." In addition, C2 did not want to be trained about all the technical details of using animals in science because she wanted to maintain her ability to react to protocols as she felt lay people would. She felt that part of her role was to appeal to community standards while combining this with a harm-benefit assessment: "My area of expertise is: 'How does the average member of the public feel about what's going on here, and does it fit within what our society views as acceptable?'—balancing the interests of the animals against the need for us to advance knowledge and understanding." Similarly, C5 described her approach as involving her, "gut reaction" to protocols, and used the "body language" of other committee members during meetings as indicators of whether she should be concerned about an aspect of the protocol.

Four members described a personal struggle between balancing their emotional and logical responses to protocols. Although T4 supported the research (from a logical perspective he saw the benefits), when describing how he reviewed protocols he described his attempt to eliminate emotions from his decisions (what types of procedures was not probed): "I try to keep my own emotions out of it, so try to keep it clear, because I certainly can get emotional when you see some of these procedures, and think, "Oh that just looks so terrible" … So—and sometimes I will admit—it's hard to keep your emotions in check." C6 described a similar experience when reviewing protocols for companion animal species: "You deal with it on the intellectual level and the emotional level ... I can look at this intellectually, and I understand it all, but when I review that, does it bother me? Yes it does."

Similarly, four members described a conflict between not liking animal-based research—seeing it as a "necessary evil"—but necessary for progress. For example, S11 working in the area of pharmaceutical development in animal models expressed a personal struggle: "I did quite a bit of animal work as a graduate student, working with rodents. And the more I worked with them, the more I hated it." Several members recounted feeling disturbed about the treatment of research animals. T2 described ending one meeting where she reviewed protocols involving neural implants: "… feeling very depressed, thinking, 'Why am I in this work? This is awful.'" C2 also described her general response to AEC work after having been on leave: "The first thing that hits you again is, 'These poor animals.'"

Different Philosophical Beliefs: Throughout the interviews, members often described their personal ethical philosophy regarding the use of animals in research. These views included ideas about rights, stewardship, sanctity of life, and the advancement of science.

C3 expressed a view aligned with some animal rights thinking, claiming that, "It is morally indefensible to use animals to promote the better health or the appearance of mere human beings." In a different vein, C2 spoke of use of animals as "a privilege, not a right." C2 also

expressed a sanctity of life view: "I can't kill a spider; I put them out the window. You know, any kind of cruelty to animals really bothers me." A community member and theologian (C4), saw his role as being a steward of animals: "They're my animals to give to these investigators, and I ask myself, 'Can I give my animals to them? Will it help the world?'" Similarly C5 believed that we, "have to respect the animal and treat and handle them correctly" in order to use them for research. Most members (27) emphasized advancement of science and seeing animals as tools to achieve this, while respecting society's (or their) concern about animal suffering.

Decisions by Precedent: Three scientist members mentioned that their decisions were aided by comparing current protocol applications to past protocols. Their knowledge of "good" protocols versus "poor" protocols gave them a reference point from which to compare current protocol application forms, much as in case law. Naturally this required the experience of being on the AEC for some time. Two scientists (S1 and S11) felt that their decision-making process was based more on personal experience than reading guidelines.

"Red Flags"

Members used certain cues in protocols as "red flags" to trigger additional attention and scrutiny, sometimes increasing the likelihood of a negative recommendation.

Discrepancies: One such cue was a discrepancy with policy or guidelines, either national or from the institution itself. For example, members cued on the use of inappropriate procedures such as in vivo monoclonal antibody production when in vitro methods were available. Another cue was a high potential for animal suffering. Technical experts, such as the animal technicians and veterinarians, also noticed procedures that they perceived to be incorrect such as an inappropriate choice of anesthetic.

Species of Animal: Fifteen members mentioned that the species of animal influenced their or their committee's decisions, either because of the species' level of sentience and capacity to suffer, or because of the value placed on different species by themselves or society. Six members mentioned that they would pay more attention to protocols using cats and dogs, either because of their own relationship with these species as companion animals, or because of perceived concern by the public about their use. For example, V2 felt that AECs needed to be sensitive to the fact that some people value companion animals more than rodents: "I would say the ones that are most contentious and therefore more difficult to approve are definitely the ones that use the companion animals, there is no question. As soon as you want to use ... a cat or a dog, then you right away have to put it into a different category in your mind." Thus, V2 felt that one needed to question the appropriateness of using these animal models, while at the same time acknowledging that a high level of sentience in rodents also requires concern.

Similarly, five members mentioned that the use of non-human primates was also a concern because of their similarity to humans in their behavior and consciousness. Although S8 approved protocols using non-human primates when he agreed that it was the appropriate model, he was uncomfortable with their use: "The more you watch them, the more you can say they are not far away from us and the more fidgety one gets about it—morally fidgety." S1 wondered if his committee was less concerned about the welfare of mice as a result of a cultural attitude towards pest species.

Comments also suggested committees should be sensitive to the emotional experiences of animal technicians working with companion animals, partially because research on

companion animals and other larger species tends to focus on individuals, thus allowing technicians or animal users to become more emotionally attached. On the other hand, seven members suggested that as long as the choice of animal model was appropriate, then they were equally concerned for the welfare of all species.

Familiarity with Investigator: Familiarity with the skills of investigators and their past interactions with the AEC played a role in how protocols were judged for 15 members. Although members generally felt that most investigators could be trusted to carry out procedures as they had outlined in their protocol application, some investigators were not trusted because the AEC had encountered problems before. Problems were usually related to lack of concern for the welfare of the animals or previous violations of standard operating procedures. Members reviewed these "problem" protocols with more scrutiny. S2 felt that familiarity with the track record of an investigator was "absolutely critical" for protocol review. As a solution, when S13's committee encountered protocols from "problem" investigators, they required these investigators to sign agreements that they would carry out modifications required by the committee.

Eight members saw animal technicians as particularly important because they are more likely to know the practices of individual investigators and can notify the AEC or the university veterinarian when they are concerned. C2 commented that animal technician members were valuable because, "They know what's going on ... the difference between the written submission of an investigator and the actual practice of the investigator, and I think that kind of input is very important." In situations where there was a concern about a particular investigator, members reported that they would sometimes request that the veterinarian or technicians monitor the situation. Moreover, the animal technicians in this study were generally less trusting of researchers than other committee members.

Quality of Completed Application Form: Eight members commented that judgments were affected by the diligence with which the investigator filled out the protocol form. Poorly filled out forms, with information missing or sloppy writing, were considered to reflect a lack of respect for the AEC oversight system. For example, S5 said that, "I will defer a protocol when basically I think it has been written without respect for the people who are going to read it and where ... the way it is written is very casual, without a lot of thinking." Similarly, T1 reported that "it's incredibly rude" for investigators to submit poorly completed applications, and that "They should be sent back, and be filled out correctly." In addition, some suggested that poorly filled out forms may also reflect poor diligence in caring for animals. For example, C4 said that, "I go through it with a fine tooth comb and say, does this person look like she will be very diligent in looking after an animal?" Likewise, C1 stated, "if you can be that sloppy with writing down some words on a piece of paper, ... are you that sloppy in the work that you do?"

Similarly, three members viewed inconsistencies in the application form as reason for a negative recommendation. Inconsistencies included whether the listed drugs matched the drugs described in procedures or whether the Category of Invasiveness matched what was expected from procedures. For example, C1 described how she searched through protocols: "I look at mortality and morbidity [percentages asked for on the form] and mostly to see if they filled it out incorrectly. Like, a lot of them write 0 for morbidity, where there's no way that is 0. ... I try to look at the medication section as to whether everything written there fits in somewhere within the procedures."

Reaching a Decision

On all four committees, members had to decide whether to: (1) unconditionally approve the protocol, (2) approve with conditions or comments, thus requiring the investigator to submit a revised protocol to the Chair and the university veterinarian, (3) defer the protocol, thus requiring a revised protocol to be resubmitted to the entire committee, or (4) reject the protocol. Most members made their final decision about a protocol after discussion and consensus at a meeting of the committee. Members often used some proportional weighting system, where the greater the number of problems or the greater the seriousness of the concerns, the greater the likelihood of withholding approval.

At University A, the majority of protocols were approved with conditions (80.3%) rather than outright (13.1%), and none were rejected; at University B and C, where discussion with investigators was encouraged before meetings, about half (53.5% and 51%, respectively) were approved outright and 0.6% and 3% were rejected (respectively). Members approved protocols with conditions when their concerns were minor and did not affect the welfare of the animals. Generally, approval with conditions resulted from missing information (e.g., missing justification of numbers or drug doses), in cases where the committee felt confident that the investigator could provide that information or add straightforward amendments.

Protocols that were deferred tended to be described as ones where there was too much missing information in order to make an evaluation. S1 felt these decisions were subjective but he felt that, "If there are enough things missing from the protocol—where I don't have a clear idea of what is going to happen to an individual animal, how long an individual animal is going to be studied ... —those are the criteria I would use for deferral." Deferred protocols also included ones where there were serious concerns about animal welfare; these included pain studies, lack of pain management after surgery, a Category of Invasiveness level E protocol without a pilot study, chronic studies, use of transgenic animals with little knowledge of side effects of transgenesis, lack of expertise by researchers, or a lack of trust in the investigator. Other deferrals resulted from lack of peer review, concerns about scientific merit or benefits of the research, or a poorly written lay summary, usually containing too much technical jargon.

Discussion

This study focused on the governance of animals within the Canadian context; however, many of the fundamental ethical issues and principles as well as procedural standards in research on animals are similar to those for research in other countries. Therefore, where applicable, the results will be discussed with respect to a broader international context.

Harm-benefit assessment (see introduction for definition) is widely regarded as the standard, analytical approach for assessing the ethical justification of experiments. It is prescribed by policy in Canada and is required by law in a number of countries including the UK, the Netherlands, Germany, and Sweden (FELASA 2007). Similar to Ideland (2009), many members in this study reported using a harm-benefit assessment, but there was large variation in how it was applied. Some members saw certain harms as unacceptable, thus trumping benefits. Members also differed in their views on which benefits helped to justify research.

Similar to a UK report (APC 2003), there was also recognition that harm-benefit assessments are inherently problematic. Although such assessments give the impression of being objective, harms and benefits are neither quantifiable nor in commensurate units, and benefits are difficult to predict. Moreover, this study suggests that harm-benefit assessments may not be an appropriate decision-making model in all cases because certain people use other

approaches, or because other considerations, not classified as benefits or harms, are also regarded as important to decision-making. In addition, a variety of ethical views, including ones based on rights and stewardship, came into play. If committees are meant to provide a broad perspective to committee discussion and decision-making, which includes public input (CCAC 2006; FELASA 2007), then greater attention to the various individual decision-making models might be necessary.

Other approaches that entered into decision-making included empathy with animals, comparison with perceived community standards, attempts to be consistent with previous decisions, and moral intuition. Emotion and moral intuition appeared to play an important role for community members, and in some cases this was combined with harm-benefit assessments. Similarly, in interviews and surveys of committee members, Galvin and Herzog (1992) found that decisions were influenced by how upsetting the experiment was to the reviewer; both rational and emotional factors were thought to interact to produce a final decision. Other studies of naturalistic decision-making have shown that people rarely use solely analytical or systematic approaches (Klein 1998; Slovic 2006).

Use of moral intuition is not unexpected given the large role of value judgments in committee decisions; "assessments of both costs to animals and benefits are matters of judgment, which, by their nature, are contestable" (APC 2003). For example, decisions about an upper limit on animal suffering is likely to invoke moral intuition that may be difficult to articulate within a rational or objective framework. For expert decision-makers, the use of "gut feel" can be a valuable tool in making decisions about complex issues (Slovic 2006). This ability is usually the result of much experience, although on the surface appears arbitrary (Klein 1998). Slovic (2006) described the Columbia Space Shuttle disaster as an example of the importance of intuition in decision-making. The disaster was a result of "failure of NASA's risk assessment protocols to give weight to the worries and hunches of personnel who had observed suspicious damage to heat-shielding tiles on previous flights." Although use of moral intuition may run counter to the ideals of rationality and objectivity—strongly valued within scientific culture—it may be an important element of committee decisions and a valuable trigger for further scrutiny of a protocol. Moral intuition might be useful for identifying ethical concerns that need further consideration, which could feed into a structured harm-benefit assessment.

The approach used to make decisions may ultimately affect the type of concerns that a committee member will consider, such as whether the Three Rs are considered. For example, the approach of reviewing a protocol from the perspective of the animal, even projecting oneself into the experiences of the animal, may result in particular attention to pain control, housing conditions, and handling (Ideland 2009). For example, Galvin and Herzog (1992) found that projection was used to both reject and approve protocols, depending on how the reviewer imagined the situation. Policy that clearly identifies the harms that AEC members should consider would help to ensure sensitivity to a wide range of possible harms (APC 2003; FELASA 2007).

Peer review by granting agencies played a large and rather poorly articulated role in the decision-making process, which has important implications for harm-benefit assessments. Here, we need to distinguish three elements that may relate to peer review: scientific merit, social value, and ethical justification. Understanding the meaning of these concepts is sometimes complicated by different terminologies and definitions that exist in the literature. The scientific merit of a project can include both scientific value (the ability of the work to make a positive contribution to advancing scientific knowledge, particularly in basic research) and the

technical merit of the proposed project (the use of testable hypotheses, good experimental design, appropriateness of the animal model and experiment for achieving the desired result, aptness of the experiment to answer the question, and skill of the investigator) (Prentice, Crouse and Mann 1992). Thus, an experiment may have high technical merit but still have low value because it contributes little of importance to scientific knowledge; technical merit can be seen as a necessary but not sufficient condition for establishing social value. Other authors, using different terms, have chosen to distinguish scientific value from technical merit (de Cock Buning and Theune 1994; Delpire, Mepham and Balls 1999; Stafleu et al. 1999). Social value has been described as the "significance of animal experimentation" (de Cock Buning and Theune 1994) and "the interest of the experiment for human beings" (Stafleu et al. 1999), while for Delpire, Mepham and Balls (1999) social value only applies to contributions to health. Many types of science are considered to have social value and hence justify animal use; these include human or animal health, basic science, environmental protection, economics, and education (Stafleu et al. 1999).

Members in this study generally took peer review as an assurance of technical merit. This fits with the purpose of peer review, although there are possible weaknesses. For example, as noted by some participants, peer review is often done at the level of an overall program, not the individual experiment, so it is possible that a weak experiment could be proposed within an overall project that has passed peer review. At a minimum, peer review should at least establish the scientist's competence to do work in the area, so it provides at least some assurance of technical merit.

Similar to respondents in a UK report (APC 2003), many members in this study took peer review as an assurance of not only technical merit but also of social value and overall justification of the proposed research. They assumed that there is no need to weigh costs to animals against benefits of the research if peer review has been done, leaving the AEC merely to assess and reduce costs. As a result, considerably less attention was paid to benefits than to costs. Acceptance of peer review as an assurance of ethical justification may represent misplaced trust because, although granting agencies differ in their procedures, in many cases peer review does not specifically ask reviewers to consider costs to animals or to balance these against social benefits. Given this interpretation of peer review by some members, there is a need either (1) to clarify the role of peer review for AECs, or (2) to expand the role of peer review so that it meets the expectation (by AEC members) that it involves an assessment of social value and overall justification, including an evaluation of costs to animals. However, even if peer reviewers assess whether the benefits of the experiment warrant the costs to animals, peer review (typically being done by scientific specialists) would lack the broader (including community-based) view that an AEC is meant to provide. If we want a broader view— including community standards—then the AEC still has to make an assessment or the peer review process needs to involve community members (US National Institutes of Health 2010). Thus, the view of some members that peer review establishes that an experiment is justified (and that the AEC should merely deal with reducing harms) is not consistent with the stated purpose of the AEC. Nevertheless, as is also recommended in the UK (APC 2003), peer reviewers could be asked to provide specific information about potential benefits that would enable committees to make better ethical decisions. Or peer reviewers could assess experimental design in the context of the Three Rs and assure AECs that the investigator had selected the minimum number of animals. One of the challenges of such an approach might be coordinating the sharing of such information.

In cases where animal harm is high or benefits are low, AEC members in this study appeared to place more emphasis on assessing justification, and seemed more likely to involve harm-benefit assessments. Similarly, in the study of Stafleu et al. (1993), researchers did not consider experiments acceptable if animal discomfort was high and social value was low. Experiments where social value was low were considered acceptable only when animal discomfort was also low. However, protocol rejection rates were low in this study as in several others done in the USA (Plous and Herzog 2001), Canada (Bowd 1997), France (Verschuere et al. 2000), and Sweden (Hagelin, Hau and Carlsson 2003; Ideland 2009). Low rejection rates may reflect, in part, a tendency of AECs to see their role as overseeing care, and reducing harms, but not as rejecting experiments, especially for protocols they take as peer-reviewed (Ideland 2009). However, low rejection rates may also suggest that the system is working well enough that investigators rarely bring poorly conceived protocols to the AEC.

Overall, in this study, criteria for the justification of research varied and assessments of ethical justification did not appear to be a major preoccupation of AEC members. Orlans (1997) and Ideland (2009) also found that AEC members did not pursue ethical review "very deeply," and other studies of AEC have found little consensus in their approach to assessing justification of research (Dresser 1989; Plous and Herzog 2001). By clarifying policy to clearly distinguish between the different components that go into decisions about the justification of research, inconsistency by members in this study and others may be reduced.

Although members in this study may not always have assessed potential benefits, they were nevertheless examining harms, and in this study and others (Dresser 1989; Stafleu et al. 1999; Hagelin, Hau and Carlsson 2003; Ideland 2009), members put a lot of effort into reducing laboratory animal pain and distress. In fact, most of the committee deliberations appeared to revolve around possible modifications to reduce pain and distress.

Members used various cues to focus their attention on specific protocols. Similarly, expert decision makers are often quite skilled at noticing cues and anomalies in patterns (Klein 1998). The species in question clearly was an important factor in decision-making (in some countries this can be driven by policy). This may sometimes fit with a harm-benefit approach, as the greater mental complexity of non-human primates may well open them to ways of suffering that do not apply to, say, fish; hence, greater care for certain species may be warranted on harm-benefit grounds. However, preferential treatment of dogs and cats may be a case where personal and community standards are being applied in a way that does not reflect a simple weighing of costs and benefits. Similarly, Galvin and Herzog (1992) found that a variety of factors related to the species of animal entered into decisions of members; these included phylogenetic considerations, capacity to suffer, labels (pet versus pest), and abundance in the wild. Although most AEC members emphasized the importance of well-justified experiments for all vertebrate species, Graham (2002) found that the use of non-human primates influenced the number of animals approved in the protocol and the diligence of assessing scientific merit.

Some of the easiest decisions of AECs occurred over the use of in vivo monoclonal antibodies or the failure to follow established Standard Operating Procedures. These were cases where there was a clear policy. In these cases, the AEC can act in a fairly straightforward and decisive manner, in contrast to difficult decisions on other issues. Having more cases of clear policy (produced by a governing body like the CCAC, or by the AEC itself) may be a major way to help AECs act decisively.

Trust in individual investigators played a key role in decision-making. Members seemed to assume that some investigators can be trusted and others cannot. Attention to potential

"problem" protocols may be a helpful safety mechanism for protecting animals. If this is so, then this is an important argument in favor of using local (rather than more centralized) institutional committees to review research protocols.

One unusual cue in this study was how well the application form was completed by investigators. This is understandable given that the committee has mainly the form to work with. It could potentially represent unwarranted trust in indirect evidence (care in completing the form taken as evidence of care in carrying out the procedures). However, scientists who attach enough importance to the AEC review process to take care in completing the form may also attach importance to following AEC requirements, so the use of indirect evidence (the form) may be warranted to a degree.

Attention to such indirect evidence may also stem from members grasping for ways to evaluate what is written on paper. One of the obstacles faced by AECs is that they have very little feedback (other that annual reports) on the ultimate effect of their decisions. Once a decision is made, for all protocols except deferrals, the majority of members do not see responses from investigators (as these typically go to the chairpersons and veterinarians). Members will visit facilities but they rarely see specific procedures. As a result, there is very little association between making a decision and learning about its outcome. Feedback is important for increasing expertise in decision-making. A more evidence-based system would not only enable AEC members to improve their ability to make good decisions, but it would also make the process more transparent and enable the public to evaluate the effectiveness of AEC decisions.

Systematic frameworks that have been developed to improve the decision-making process of AECs (Smith and Boyd 1991; Porter 1992; de Cock Buning and Theune 1994; Mellor and Reid 1994; Stafleu et al. 1999; APC 2003) are likely to increase objectivity, transparency, and consistency in decisions, all of which are valued goals of the review process (CCAC 1997). In a similar fashion, Plous and Herzog (2001) suggested that consistency could be improved by adopting approaches recommended for editorial peer review: developing specific evaluative criteria, decomposing global ratings into smaller categories, and averaging across multiple judgments. Systematizing decisions will likely help to ensure that all morally relevant concerns are raised. For example, several frameworks could be used to assess benefits and scientific quality more systematically than was done by the committees studied here (Smith and Boyd 1991; de Cock Buning and Theune 1994; Stafleu et al. 1999). Other factors, such as trust in investigator, not traditionally considered a part of protocol review, may also need to be recognized as valuable information. These frameworks can also provide a mechanism for discussion without necessarily turning the process into an exercise of calculation (de Cock Buning and Theune 1994; Stafleu et al. 1999).

The disadvantage of these frameworks is that they tend to emphasize a single mode of decision-making (often harm-benefit assessment), and thus do not leave much scope for other approaches such as moral intuition. Hence, they may invalidate how some (especially non-scientist) members naturally make decisions. If these members feel marginalized already, then this will further reduce their contribution (Schuppli and Fraser 2007). Indeed, results of this study support the observation by Galvin and Herzog (1992) that people use different patterns of moral reasoning. In addition, given the complex relationship between peer review by AECs and funders, it may be difficult to carry out accurate harm-benefit assessments. There may be a need, both in policy and in the conduct of AEC meetings, to clarify the place and validity of alternate ways of making decisions. For example, committees may need to be responsive to views expressed in emotional terms. In order to make decisions more systematic (and thereby

hopefully more consistent), it may be preferable to set out the information required rather than the logic (weighing of harms and benefits) to be applied to the information. Decisions will still involve individual judgment, but the information that goes into the decisions may be more consistent. One potential advantage of consensus-based decision-making by committees is that any shortcomings of individual decision-making may be overcome by group input into the final decision. However, committees must also be vigilant to potential shortcomings of group decision-making—committee structure, social influences, and recruitment processes leading to biases or polarization (Schuppli and Fraser 2007).

In summary, although most policy assumes, recommends, or requires a systematic harm-benefit assessment for making decisions about animal use, many AEC members use other approaches. These include empathy with animals, comparison with perceived community standards, attempts to be consistent with previous decisions, and moral intuition. Thus, imposing logical systems based on a systematic harm-benefit assessments may not be suitable, especially for non-scientist members. If we want a broader view—including community input—the door is open, not only for other standards, but also for other styles of making decisions. Decisions will require that all relevant information is provided but how the decision is made could vary. Expertise in decision-making could also be improved if members received more evidence on the outcomes of their decisions.

The relationship between AEC and funding-body peer review needs to be clarified, ideally through discussion between these two groups. In particular, clarity is needed on the elements of scientific merit and social value, and on which review process covers which elements. However, the AEC should not be bound by peer review because it does not offer the same assurances (notably community input) that the AEC brings.

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References

APC. 2003. *Review of Cost-Benefit Assessment in the Use of Animals in Research. Report of the Cost-Benefit Working Group of the Animal Procedures Committee.* London: Home Office, Communication Directorate.

Bowd, A. D. 1997. The educative role of an animal care committee in Canada: A case study. *Animal Welfare* 6: 309–315.

CCAC. 1993. *Guide to the Care and Use of Experimental Animals*. Ottawa, Canada: Canadian Council on Animal Care.

CCAC. 1997. *CCAC Guide to Protocol Review*. Ottawa, Canada: Canadian Council on Animal Care.

CCAC. 2006. *Terms of Reference for Animal Care Committees*. Ottawa, Canada: Canadian Council on Animal Care.

de Cock Buning, T. and Theune, E. 1994. A comparison of three models for ethical evaluation of proposed animal experiments. *Animal Welfare* 3: 107–128.

Delpire, V. C., Mepham, T. B. and Balls, M. 1999. A proposal for a new ethical scheme addressing the use of laboratory animals for biomedical purposes. *Alternatives to Laboratory Animals* 27: 869–881.

Dresser, R. 1989. Developing standards in animal research review. *Journal of the American Veterinary Medical Association* 194: 1184–1191.

European Biomedical Research Association. 2010. Laboratory animal research legislation in Sweden. <http://www.ebra.org/sweden+1_17.htm/> Accessed on August 28, 2010.

FELASA. 2007. Principles and practice in ethical review of animal experiments across Europe: Summary of the report of a FELASA working group on ethical evaluation of animal experiments. *Laboratory Animals* 41: 143–160.

Galvin, S. L. and Herzog, H. A. 1992. The ethical judgment of animal research. *Ethics and Behavior* 2: 263–286.

Graham, K. 2002. A study of three IACUCs and their views of scientific merit and alternatives. *Journal of Applied Animal Welfare Science* 5: 75–81.

Hagelin, J., Hau, J. and Carlsson, H. E. 2003. The refining influence of ethics committees on animal experimentation in Sweden. *Laboratory Animals* 37: 10–18.

Ideland, M. 2009. Different views on ethics: How animal ethics is situated in a committee culture. *Journal of Medical Ethics* 35: 258–261.

Klein, G. 1998. *Sources of Power: How People Make Decisions.* Cambridge: MIT Press.

LeCompte, J. J. and Schensul, M. D. 1999. Designing and conducting ethnographic research. In *Ethnographer's Toolkit, Vol. 1*, 240, ed. J. J. LeCompte and M. D. Schensul. Walnut Creek, CA: Rowman Altamira.

Mellor, D. J. and Reid, C. S. 1994. Concepts of animal well-being and predicting the impact of procedures on experimental animals. In *Improving the Well-Being of Animals in the Research Environment,* 3–18, ed. R. M. Baker, G. Jenkin and D. J. Mellor. Glen Osmond, Australia: ANZCCART.

Orlans, B. F. 1997. Ethical decision making about animal experiments. *Ethics and Behavior* 7: 163–171.

Plous, S. and Herzog, H. 2001. Reliability of protocol reviews for animal research. *Science* 293: 608–609.

Porter, D. G. 1992. Ethical scores for animal experiments. *Nature* 356: 101–102.

Prentice, E. D., Crouse, D. A. and Mann, M. D. 1992. Scientific merit review: The role of the IACUC. *Institute for Laboratory Animal Research News* 34: 15–19.

Russell, W. M. S. and Burch, R. L. 1959. *The Principles of Humane Experimental Technique.* London: Methuen.

Schuppli, C. A. 2007. Factors influencing the effectiveness of research ethics committees. *Journal of Medical Ethics* 33: 294–301.

Schuppli, C. A. and Fraser, D. 2005. The interpretation and application of the Three Rs by animal ethics committee members. *Alternatives to Laboratory Animals* 33: 1–14.

Slovic, P. 2006. Affect, reason, risk and rationality. *Newsletter of the European Working Group Multicriteria for Decisions* 3: 1–5.

Smith, J. A. and Boyd, K. M. 1991. *Lives in Balance. The Ethics of Using Animals in Biomedical Research.* Oxford: Oxford University Press.

Stafleu, F. R., Baarda, B. D., Heeger, F. R. and Beynen, A. C. 1993. The influence of animal discomfort, human interest and scientific quality on the ethical acceptability of a projected animal experiment as assessed with questionnaires. *Alternatives to Laboratory Animals* 21: 129–137.

Stafleu, F. R., Heeger, F. R. and Beynen, A. C. 1989. A case study on the impact of clinically-observed abnormalities in mice with gallstones on the ethical admissibility of a projected experiment with gallstone-bearing mice. *Alternatives to Laboratory Animals* 17: 101–108.

Stafleu, F. R., Tramper, R., Vorstenbosch, J. and Joles, J. A. 1999. The ethical acceptability of animal experiments: A proposal for a system to support decision-making. *Laboratory Animals* 33: 295–303.

US National Institutes of Health. 2010. Peer review process: Grants Process of the Office of Extramural Research. <http://www.grants.nih.gov/grants/peer_review_process.htm> Accessed on August 28, 2010.

Verschuere, B., Autissier, C., Degryse, A. D., Gallix, P., Gotti, B., Laurent, J., Leinot, M. and Peyclit, I. 2000. Ethics committee recommendations for laboratory animals in private research in France. *Laboratory Animals* 34: 236–243.