

- c. The present e-Sirius animal ordering and business functions are a strength of the system and should be maintained.
2. Reinstitute the veterinary consultation/pre-review in the protocol development phase. The incorporation of the veterinary pre-review with the e-Sirius protocol submission has delayed the veterinary input to protocol development to where it is perceived of as more of a hindrance than a benefit. This review should be interactive with discussion among the investigator and the veterinarian, not anonymous as it is presently established.
3. Consistency in animal use protocol review requires that reviewers interact and discuss the new issues associated with animal use protocol reviews. Expansion of the interactions and educational activities, both formal and informal, among the veterinary staff and the IACUC members would enhance the exchange of ideas and improve consistency in animal protocol review.

The basis for this consensus recommendation of the committee is presented in the attached final report. We hope that the report provides the factual evaluation of the animal use protocol system and process that you requested and serves as a starting point for improving the animal use protocol system.

If you would like to sit down with the committee and discuss the findings and recommendations of the committee in more detail, I would be happy to arrange the meeting.

Sincerely,



Harold F. Stills, Jr., DVM
Director, Division of Laboratory Animal Resources and
Professor of Microbiology, Immunology, and Molecular Genetics
Chair, *ad hoc* Committee on Animal Use Protocols

cc: *ad hoc* Committee members

enc.

Report of the *ad hoc* Committee on Animal Use Protocols

On September 15, 2008 the *ad hoc* committee on animal use protocols was established with the charge of evaluating and making recommendations regarding the animal use protocol process. Specifically, the *ad hoc* committee was charged with: 1) evaluation of the e-Sirius protocol submission and review process, 2) evaluation of the logistics of animal use protocol processing, and 3) evaluation of the review process of the IACUC.

The *ad hoc* committee membership was comprised of veterinarians involved in animal care, IACUC members, and faculty actively involved in animal research and representing the major University Colleges using vertebrate animals. Committee membership consisted of Drs. Harold F. Stills, Jr. (Attending Veterinarian and Committee Chair), Susan Barron (Psychology), Sandra J. Bortnick (DLAR Veterinarian), Alan Daugherty (Cardiovascular Medicine), David L. Harmon (Animal & Food Science), Eric J. Smart (IACUC Member, Pediatrics), Brett T. Spear (Microbiology & Immunology), and Sidney Whiteheart (IACUC Chair, Biochemistry).

The *ad hoc* committee met multiple times from September 2008 through January 2009 to discuss the objectives and develop approaches to address the committee's charge. The approaches employed by the committee included: 1) direct discussions between committee members and individual or small groups of faculty, 2) collection and analysis of data regarding protocol processing times, 3) contact with individuals (veterinarians, IACUC staff, and faculty) at other Institutions using e-Sirius® or other animal use protocol processes to solicit their overall impressions and recommendations, and 4) development and deployment of a survey instrument to solicit faculty input regarding the protocol submission process, veterinary review of protocols, and IACUC protocol evaluation (a copy of the survey instrument, the survey results, and all faculty survey comments is attached). The committee met and discussed the responses received and arrived at the findings regarding the charge as detailed below.

Evaluation of the e-Sirius® protocol submission and review process

The e-Sirius® animal use protocol system is a server-based database system that is both secure and accessible from any location with internet access. The database nature of the system permits a "branching" type of interface with data screens becoming available based upon responses. This type of system generally requires a mandatory response to specific questions to permit the generation of the appropriate screens for completion of the animal use protocol. The order that the information is entered lacks some degree of flexibility due to the nature of the program. The database system also permits extensive querying of the information entered for reporting or documentation purposes.

The e-Sirius® animal use protocol submission system was a focus of faculty researcher dissatisfaction. This was evident in the results from the survey, from individual faculty comments on the survey, and from individual meetings between committee members and faculty researchers.

1. Regulatory Requirements and the e-Sirius® Protocol Submission Process:

One of the purported strengths of the e-Sirius® protocol system is regulatory compliance. The database format allows the designation of certain fields as mandatory fields, requiring the investigator to complete the field prior to protocol submission for review. This feature significantly reduces the potential of protocol approval without the completion of sections that are mandated by regulations. The database system retains detailed records of all activities related to protocol submission, review, changes, and approval permitting documentation of the review procedures, practices, and communications. There have been no reports of a noncompliance attributable to the e-Sirius® protocol submission system.

The e-Sirius® protocol system was designed with the documentation of regulatory compliance as a primary focus. Implementation of the system, however, has a significant effect upon regulatory compliance and the e-Sirius® protocol submission and review system has been implemented in several different variations. The *Animal Welfare Regulations* (9 CFR, Chapter 1, Subchapter A) and the *Public Health Service Policy on Humane Care and Use of Laboratory Animals* provide two acceptable methods of animal use protocol review and approval by the IACUC, Designated Review and Full IACUC Review. Additionally, the Animal Welfare Regulations require that “procedures that may cause more than momentary or slight pain or distress to the animals will: (B) Involve, in their planning, consultation with the attending veterinarian or his or her designee;” (9 CFR §2.31 d, 1, iv)

Of the 5 institutions using e-Sirius® for protocol submission that responded to a request for information, several different variations of the e-Sirius® protocol system were described. Two of the institutions performed a veterinary pre-review prior to submission of the protocol to the IACUC for full review. The remaining 3 institutions did not use a veterinary pre-review and used the Designated Review system for all protocols (2) or all protocols except for those with animals in USDA category E (unrelieved pain and distress) studies (1). In these later three cases, a veterinarian was always included as one of the designated reviewers.

2. The e-Sirius® Protocol Submission Process:

Faculty consensus was that the e-Sirius® system, as presently implemented, is laborious, confusing, complicated, redundant, unfriendly for users, and impairs faculty research productivity. Navigating the protocol submission screens is tedious and prevents the investigator from seeing the entire protocol at one time. The protocol submission platform lacks basic features such as “spell checking” and the “track changes” features that are expected in word-processing software. The inability to include tables or graphic items in the protocol system without using attachments impairs both the description of the research effort by the faculty and the review of the proposed animal research by the veterinarians and the IACUC. The program mandated questions lack clarity and often are redundant. The confusing order of the questions and the inability to easily navigate between different sections further complicates the process. Repetitive entering of similar information into different sections requires additional faculty

effort, increasing frustration with the system while providing no increased value in animal protocol evaluation.

Individuals directly involved with e-Sirius® from five other institutions (IACUC staff, veterinarians, *etc.*) were contacted and responded to our inquiries. Four of the five institutions characterized the level of satisfaction of faculty researchers with the e-Sirius® animal use protocol system as not very satisfied or poor satisfaction. The only institution that did not report a low level of satisfaction had just initiated the use of e-Sirius® for their protocol submission in November 2008. One of the five institutions presently using e-Sirius® for animal use protocol processing has already opted to abandon the e-Sirius® system due to faculty and staff dissatisfaction with the system.

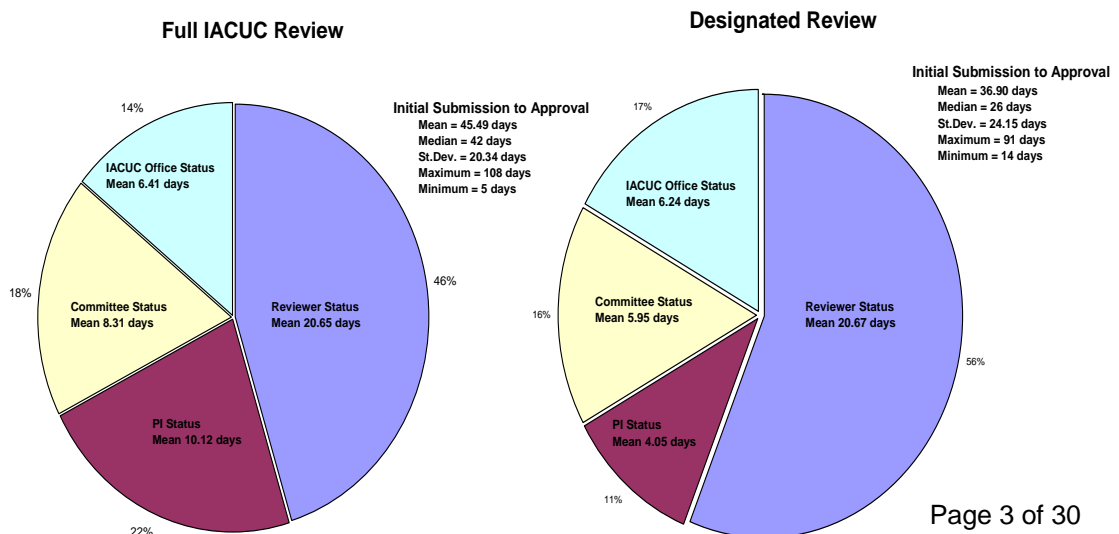
3. The e-Sirius® Animal Ordering, Billing, and Reporting Systems:

In contrast, the e-Sirius® animal ordering, animal inventory tracking, fiscal management, and reporting systems were generally regarded as excellent and beneficial by both the research faculty at the University of Kentucky and at other institutions. A number of faculty researchers, while severely criticizing the protocol submission and review process, praised the efficiency and ease of the animal ordering and fiscal tracking components of the e-Sirius® package. Several faculty researchers and a number of surveyed institutions using e-Sirius® listed a perceived increase in compliance as a benefit while others listed the required inclusiveness of the protocol form and the ability to generate compliance reports as beneficial.

Evaluation of the logistics and processing times of animal use protocols

1. Protocol Processing Times:

The time required for animal use protocol processing was determined by reviewing all new and *de novo* third year protocols reviewed by the IACUC from April 1, 2008 through October 1, 2008. The mean time from initial submission to approval was 45 days for protocols reviewed by the Full IACUC. This approval period was reduced to a mean of 37 days for protocols eligible for and reviewed by Designated Review. The only significant difference in review time requirements between Full IACUC Review and Designated Review involved the



amount of time required for principal investigator corrections and responses which increased from approximately 4 days to 10 days, presumably due to the more complicated nature of animal use protocols referred for Full IACUC Review. The average time from investigator submission to full protocol approval at other institutions was extremely variable and highly dependent upon the level and type of protocol review. Several of the institutions already using e-Sirius® for protocol review have elected to use Designated Review for all protocols, with reported completion times ranging from 2 weeks to 2 months. One institution reported a processing time of 4-6 weeks while another reported an average of 53 days for approval. Finally, the institution that has opted to abandon the e-Sirius® system reported a submission to approval time range of 8-10 weeks.

Faculty researchers at the University of Kentucky did not indicate that the time from submission to approval was a significant issue. The average faculty response to the statement "The overall IACUC protocol review and approval process was much slower than what would be expected" was 3.5 on a 1 (strongly disagree)-5 (strongly agree) scale, with more senior faculty more likely to strongly agree with the statement. Additionally, when asked if they agreed with the statement that the protocol approval process was appropriate, the average response was a neutral 2.7 (same 1-5 scale), with the senior faculty more likely to disagree with the statement.

2. Logistics of Animal Use Protocol Processing:

New and third year *de novo* animal use protocols are processed by either designated review (when no pain or distress is anticipated - USDA classifications B and C) or by full IACUC review (when pain or distress is anticipated - USDA classifications D and E). All animal use protocols are reviewed by both a veterinary reviewer and a scientific reviewer with suggestions, comments, and requested clarifications communicated anonymously to the principal investigator through the IACUC office staff. A flow-chart diagramming the typical animal use protocol processing for both Full IACUC Review and for Designated Review is attached.

All submitted new and third year *de novo* protocols are first reviewed for omissions and major errors by IACUC staff from the Office of Research Integrity. Following this administrative staff review, veterinary and primary reviewers are assigned by the administrative staff and the protocol is posted for pre-review. Prior to October 2008, animal use protocols destined for full IACUC review were submitted for a seven day veterinary and primary reviewer pre-review prior to being posted for 5 days on e-Sirius® for each IACUC member to review. After October 2008, the veterinary and primary reviewer pre-review was incorporated with the e-Sirius® posting to all IACUC members, reducing the protocol processing time.

Annual protocol reviews and significant amendments to protocols are processed using the designated review system. Following administrative review by the IACUC staff, a single reviewer is assigned for annual reviews while significant amendments are assigned to both a scientific and veterinary reviewer. These submissions are posted for IACUC member access on the e-Sirius® system for a

minimum of 5 business days, during which time they are also available to the reviewer(s).

Faculty investigators were aware of the overall general protocol system but they were not familiar with the specifics. Most faculty investigators did not differentiate the “pre-review” of the protocol by the veterinary and scientific reviewers from the IACUC review of the protocol. Many were left with the impression that the comments and suggestions generated in the pre-review process were mandatory IACUC-mandated changes and not suggestions or inquiries from the preliminary reviewers designed to assist in obtaining IACUC approval. This situation was exacerbated by an e-Sirius[®] system requirement of a response to a reviewer comment with no apparent means of rebuttal. The use of an anonymous reviewer system further prevented the faculty researchers from contacting the reviewers directly to discuss and resolve issues with the end result of protocol delays and frustration.

Evaluation of the IACUC review process

1. The IACUC Preliminary Review Process:

The use of an anonymous reviewer system and the veterinary “pre-review” process were topics that were repeatedly criticized by faculty researchers. While the overall faculty evaluation of the quality and appropriateness of the questions and comments received during the review process was in the average range (3.0 and 2.8 respectively on a 1-5 scale), a number of faculty made the effort to provide thoughtful and detailed written comments regarding these two issues.

Consistency of the veterinary reviewer comments and frustration with differing veterinary review comments was a common complaint. Many investigators commented that they received disparate reviews depending on the particular veterinarian to which the protocol was assigned. In some cases, particular sections mandated by one veterinarian required alteration during annual or third year *de novo* reviews by a different veterinarian. Instances where veterinary reviewers required major alterations during the annual protocol review was a particularly frustrating aspect of the system to investigators. Changes in pain classifications during annual and *de novo* reviews was another area of investigator contention listed multiple times.

A number of faculty researchers complained or commented about the anonymity of preliminary reviewers. The anonymity of the reviewers was associated with an inability of the investigator to directly respond to the reviewer’s comments and frequently listed as preventing open communication and as counterproductive. Together, the two issues of inconsistencies in review and anonymity of the reviewers appeared to be responsible for a significant portion of the frustration of faculty researchers responding to the survey. In contrast, faculty researchers that were directly contacted by the veterinarian or primary scientific reviewer during the “pre-review” rated the direct contact to be very beneficial (4.7 on a 1-5 scale).

2. IACUC Guidance to Investigators:

As a component of the survey, faculty researchers were asked to rank the perceived benefit of a number of potential “improvements” in the e-Sirius[®] protocol submission process. The proposed “improvements” included additional training regarding protocol submission and processing, revising the questions in e-Sirius[®] to improve clarity, and the inclusion of links to additional examples, regulations, and policies and procedures.

- a. The provision of additional training on using e-Sirius[®] and on the overall protocol submission and approval process was not perceived as being of great benefit, especially by the more senior investigators.
- b. The inclusion of references to the regulatory basis for specific questions or sections in the animal use protocol form was also perceived as being of little benefit.
- c. The publishing and availability of examples of IACUC reviewed and approved standard procedures was listed as potentially very beneficial and was frequently listed as an area where significant improvement could be made. The easy availability of commonly used procedures for copying and inclusion into new animal use protocols was perceived as a method to increase compliance while shortening approval times and easing the demands upon the faculty researchers and the IACUC reviewers.

Similarly, the provision of links to recommended policies, practices, and procedures was perceived as potentially very beneficial. Links to surgery recommendations, recommendations for anesthesia, analgesia, and euthanasia, as well as links to end-point recommendations were all evaluated as beneficial to very beneficial.

- d. Lastly, faculty researchers were asked to evaluate the potential benefit of expanded and earlier involvement of the veterinarians in protocol development of pre-review. The ability to contact and involve the veterinarians in early protocol development along with the ability to submit early draft versions of the protocol for veterinary input were both considered as beneficial improvements. There was a neutral faculty researcher response to making the veterinary pre-review mandatory.

Conclusions and Recommendations

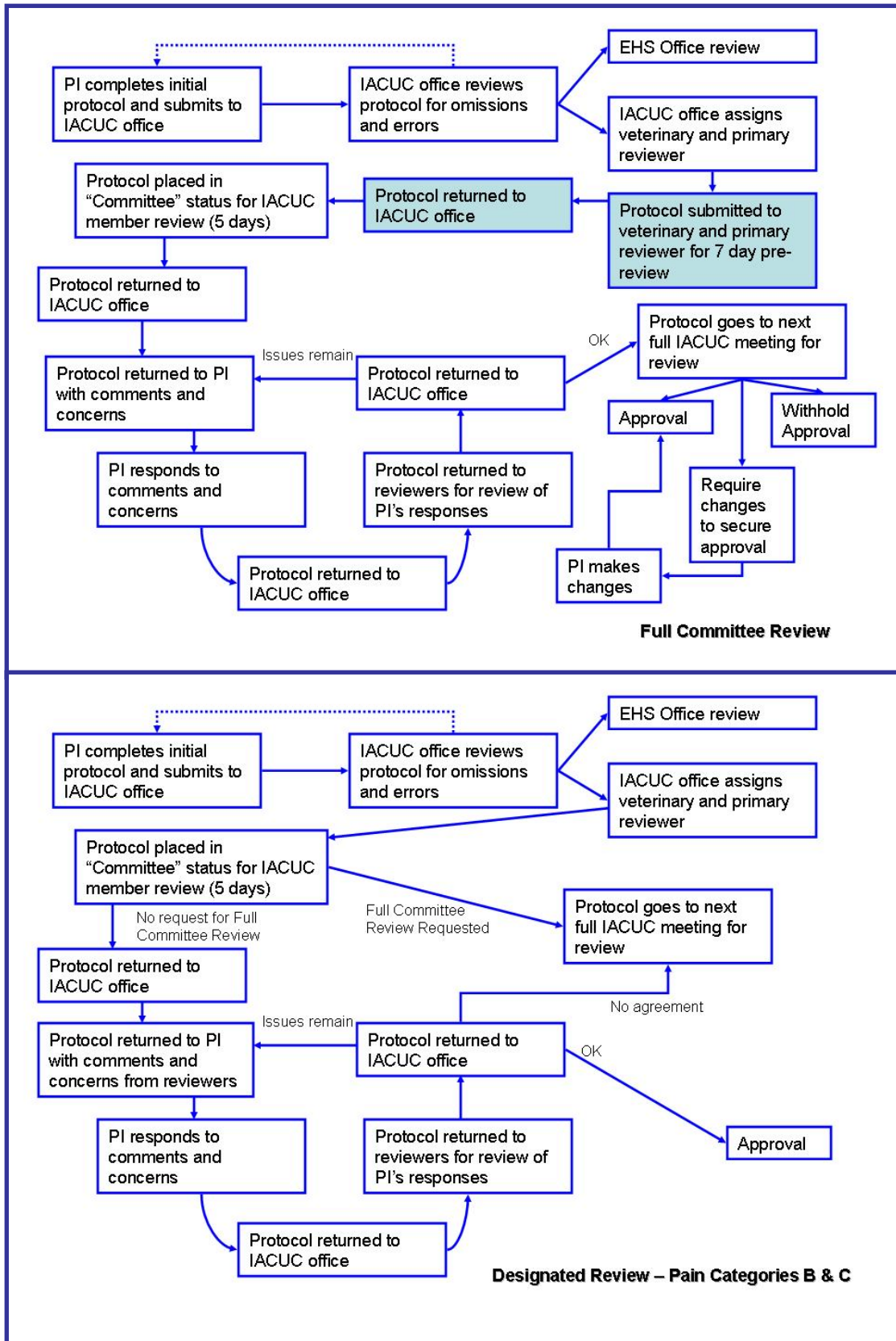
- No clearly superior protocol submission-animal facilities management system is commercially available at this time. Each system has particular strengths and weaknesses that become apparent during system implementation.
- The use of the e-Sirius[®] interface for protocol submission should be either extensively modified or completely replaced. While the e-Sirius[®] system has a number of excellent features, the protocol submission interface used by the investigator is poorly designed, cumbersome, difficult to use, and counterproductive to the research mission of the University of Kentucky. The

replacement of the e-Sirius[®] interface with either Microsoft Word-based forms or Adobe Acrobat forms could be a significant improvement and provide the faculty researchers with a familiar interface. The logistics of such a switch would require extensive planning and preparation to ensure a smooth transition while maintaining compliance with the regulations and compatibility with existing e-Sirius[®] systems for animal ordering, documentation, and report generation. The transition, implementation, and maintenance of the system might also require additional office support staff in the Office of Research Integrity.

- Establish a committee or working group to review and modify the present e-Sirius[®] protocol submission form. The present protocol submission form contains a number of marginal questions providing little or no value in IACUC protocol review or report generation while serving as a significant source of faculty frustration with the system. The redrafting of questions to improve clarity and the inclusion of examples and “boiler-plate” protocol statements would also be beneficial to the present protocol submission system. This interim step would be of immediate value to the faculty researchers during the period when the e-Sirius[®] protocol interface is being either extensively modified or replaced and would serve as a basis for determining the information requirements for the new interface.
- Maintain the present e-Sirius[®] system for animal ordering and business functions. This system is generally well-liked by both the faculty investigators and the animal care personnel. The system is also highly integrated into IACUC functions, animal numbers tracking, and report generation for both regulatory and accrediting bodies.
- Reinstitute the veterinary consultation/pre-review. Consultation and communication between the veterinarians and the faculty researchers is an important aspect of the entire protocol development and implementation process. The unique and special expertise of the veterinarian can be a valuable asset in experiment design and performance when a collegial relationship exists. The present “pre-review” occurs after the investigator has essentially completed the entire protocol. Veterinary assistance, suggestions, and recommendations that could have improved the protocol while saving faculty investigator effort if provided earlier in the process, are now thought of as unnecessary, obstructionist, and of little value. The veterinary pre-review should be reinstated prior to submission of the protocol to the IACUC and the consultation should be directly between the faculty investigator and the responsible veterinarian.
- Continue and expand educational activities and discussions among the veterinary staff and the IACUC members regarding controversial aspects of animal use protocol review. Consistency of the protocol review was a significant area of contention unrelated to the actual protocol processing system. Efforts already initiated to bring consistency to the veterinary and IACUC reviews should be expanded and continued. Veterinary review consistency is primarily the responsibility of the attending veterinarian and can be enhanced by continued meetings and discussions among the veterinary staff regarding the veterinary aspects of the protocol review. Consistency in IACUC protocol review requires increased education of the IACUC members on the regulatory requirements

required for animal use protocol review, the establishment of reasonable expectations by the IACUC, and the communication of the expectations through published IACUC Policies and Procedures and other means.

Animal Use Protocol Processing Flow



SharePoint On-Line Survey Form

[DLAR](#) > [eSirius On-line Survey](#) > Respond to this Survey

eSirius On-line Survey: Respond to this Survey

Please select the range below that includes your age.

- <30 years old
- 30-40 years old
- 40-50 years old
- 50-60 years old
- >60 years old

Please circle the choice below that best describes your academic rank.

- Research Associate
- Assistant Professor
- Associate Professor
- Professor
- Departmental Chair or Unit Director

Please indicate the range below that best describes the number of years you have been at the University of Kentucky.

- <1
- 1-2
- 2-5
- 5-10
- >10

Please indicate the number of presently active animal use protocols where you are the principal investigator.

- 1
- 2
- 3-5
- >5
- 0

Please indicate the number of presently active animal use protocols where you are a co-investigator.

- 1
- 2
- 3-5
- >5
- 0

Section 1. e-Sirius PROTOCOL SUBMISSION PROCESS: Animal use protocols are initially completed by the principal investigator, submitted to the IACUC office, and then subjected to multiple levels of review and comment prior to approval by the IACUC. The following questions address the ease of using the e-Sirius on-line protocol system when initially preparing and submitting your animal use protocol. . . . On a scale of 1 to 5, how would you rate...

	Poor 1	Average 2	Average 3	Excellent 4	Excellent 5
..... the instructions and guidance you were provided?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
..... the clarity of the questions in the e-Sirius protocol submission system? Did you know what specific information was being requested in each section?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

..... Were the requests for information logically ordered?

Did you contact either the Office of Research Integrity IACUC staff or the DLAR veterinary staff for assistance with preparing the e-Sirius protocol form?

- Contacted ORI IACUC staff
- Contacted DLAR veterinary staff
- Got help from others (faculty, staff, etc.) in completing the form
- Did not know who to contact and did not get help though it was needed
- Did not need any help

Section 2. e-Sirius PROTOCOL PRELIMINARY REVIEW PROCESS: Each animal use protocol undergoes an initial preliminary review, usually by an IACUC member and a veterinarian, prior to submission to the IACUC for review and evaluation. This review generally results in a number of questions, concerns, requests, etc. from the reviewer(s) that are returned to the principal investigator to be addressed in a protocol revision. This process may be repeated multiple times as the protocol is revised for submission to the IACUC for final approval. The time required for the initial preliminary review is quite variable depending upon the complexity of the protocol, the time of submission, and the workload upon the IACUC and veterinary reviewers. The following questions address this aspect of the protocol review and approval process. Please rate ...

	Poor		Average		Excellent
	1	2	3	4	5
..... the quality of the questions, concerns, and comments that were returned to you. Did you understand what the reviewer was requesting?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
..... the appropriateness of the questions, concerns, and comments that	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

were returned to you. Did you consider the comments reasonable and justified?

While the e-Sirius system is designed primarily for anonymous electronic communication between the investigator and the reviewers, individual reviewers may initiate direct contact with the investigator. Have you ever been contacted directly, by e-mail, telephone, or in person, by one of the reviewers during the review process?

- YES
- NO

If you were directly contacted, please rate...

	Little benefit		Useful		Very beneficial
	1	2	3	4	5
... the effectiveness and benefit of the direct individual contact	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Section 3. IACUC PROTOCOL REVIEW: After the preliminary review process is completed, animal use protocols are routed to the IACUC and may be reviewed and approved by one of two methods. Animal use protocols that involve no or minimal pain and distress are reviewed by 2 IACUC members using a designated reviewer system. Animal use protocols involving greater than slight or momentary pain and distress are reviewed by the full IACUC at a scheduled monthly convened meeting of the committee . . . The following questions address this final review and approval process: . . . Did the IACUC review raise any additional questions about your protocol that were not covered in the preliminary reviews?

- YES
- NO

If yes, please rate ...

Poor Average Excellent

	1	2	3	4	5
..... the appropriateness of the questions that were returned to you; were the questions and/or requests reasonable and justified?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
..... the time required for receipt of final IACUC approval	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Section 4. OVERALL IACUC PROTOCOL REVIEW AND APPROVAL PROCESS: Please indicate your level of understanding/agreement for the following two statements:

	Strongly Disagree 1	2	Neutral 3	4	Strongly Agree 5
..... STATEMENT 1--- The OVERALL IACUC protocol review and approval process was much slower than what would be expected.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
..... STATEMENT 2 --- The OVERALL IACUC protocol review and approval process was appropriate.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Section 5. IMPROVING THE PROTOCOL PROCESS: Your comments in this section are critical to improving the process. Please evaluate the perceived value of the following changes from your perspective as an investigator submitting an animal use protocol for IACUC review and approval.

	Little value		Useful		Very valuable
	1	2	3	4	5
.....Providing additional training regarding protocol processing;	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....Providing additional training in the use of e-Sirius system;	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....Personnel available for assistance to investigators, especially new investigators, in understanding and completing the process	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

2-- Revising or writing questions in the e-Sirius form to

	Little value		Useful		Very valuable
	1	2	3	4	5
..... improve clarity;	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....expand descriptions of information requested;	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
..... cite regulatory basis for the request;	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
..... include examples of acceptable responses.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

3-- Providing links in the e-Sirius form to

	Little value		Useful		Very valuable
	1	2	3	4	5
..... IACUC Policies and Procedures;	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

..... Recommendations for anesthesia, analgesia, and euthanasia;	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
..... Tumor endpoints, tissue collection for genotyping, etc.;	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
..... Requirements for survival and non-survival surgical procedures;	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
..... Providing the option for investigators to request direct, individual assistance and consultation with a veterinarian during the early stages of protocol development prior to submission to the IACUC	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

4-- Establishing a mandatory veterinary preliminary review prior to submission of animal use protocols

	Little value 1	2	Useful 3	4	Very valuable 5
..... where more than momentary pain or distress is anticipated.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

5-- Reconfiguring the e-Sirius system

	Little value 1	2	Useful 3	4	Very valuable 5
..... to facilitate submission of a draft protocol for pre-review by the	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

veterinary
staff.

If you have familiarity with a different animal use protocol system at another Institution, would you please provide some comments comparing the University of Kentucky e-Sirius system to the system at the other Institution. Comments addressing thoroughness of the questions, ease of protocol completion, review interactions, and approval time would be greatly appreciated.



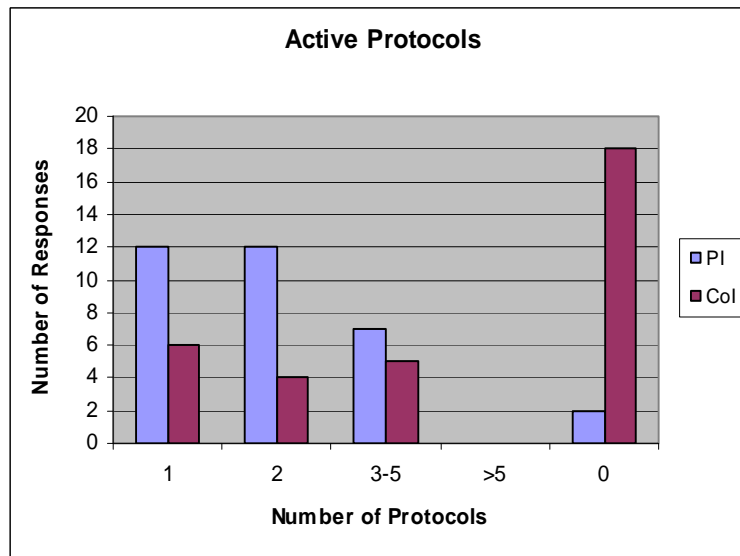
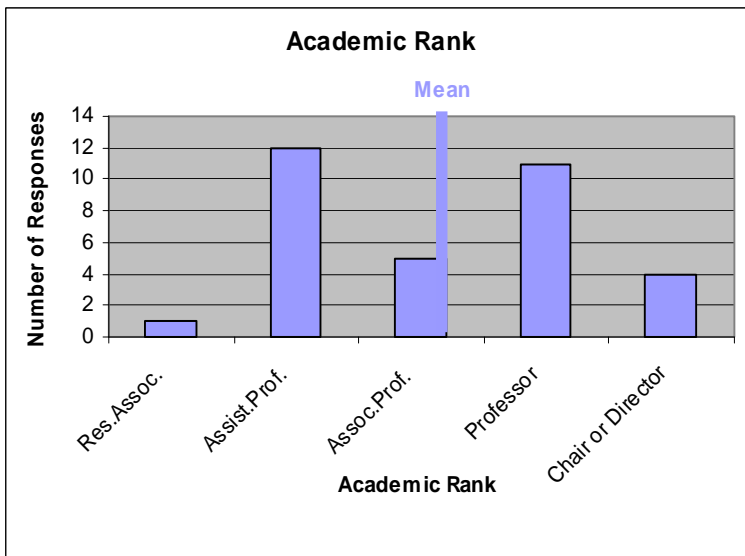
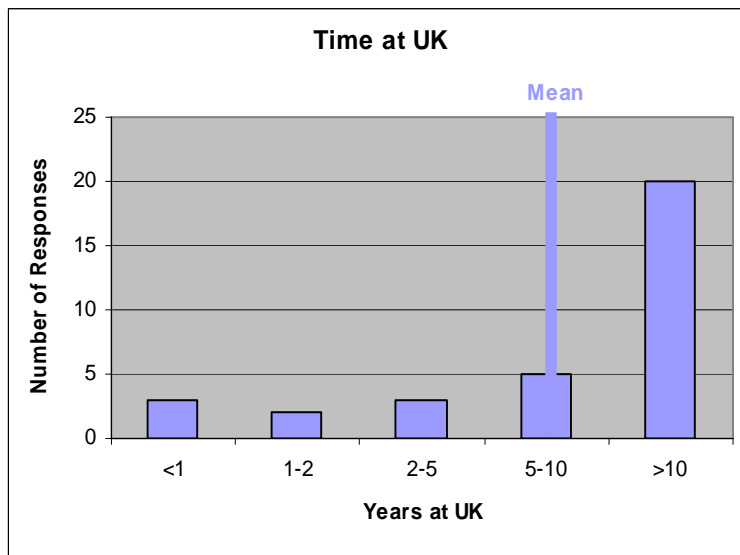
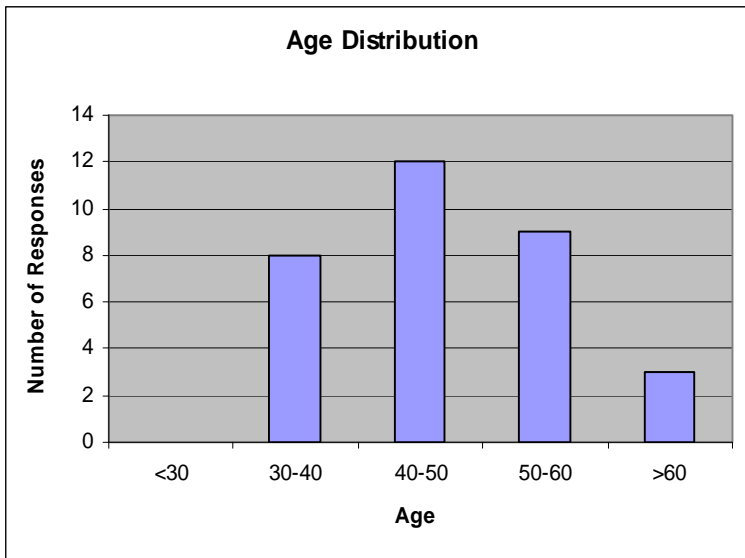
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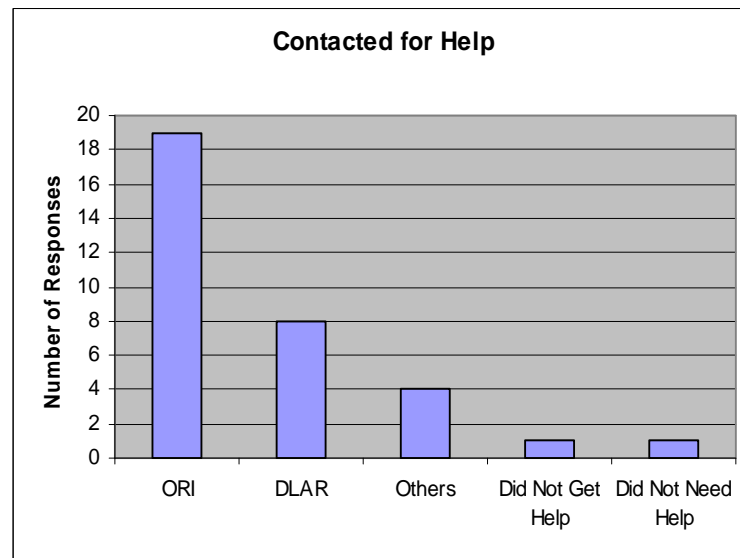
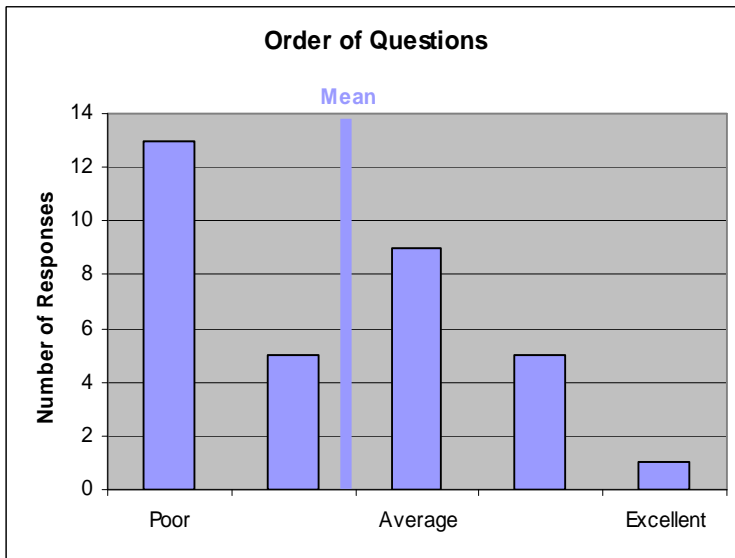
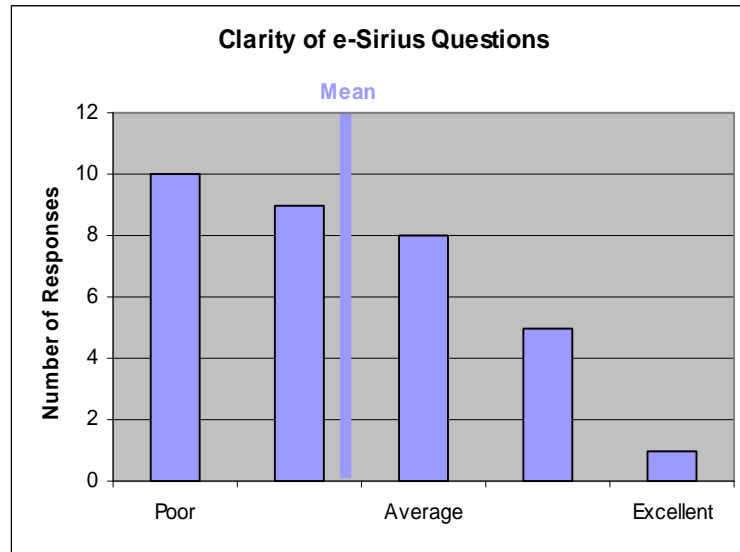
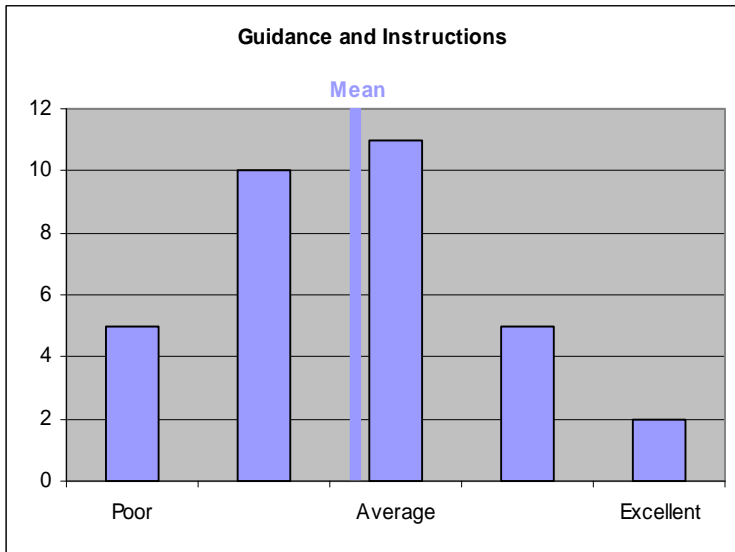
Other comments or recommendations would be greatly appreciated:

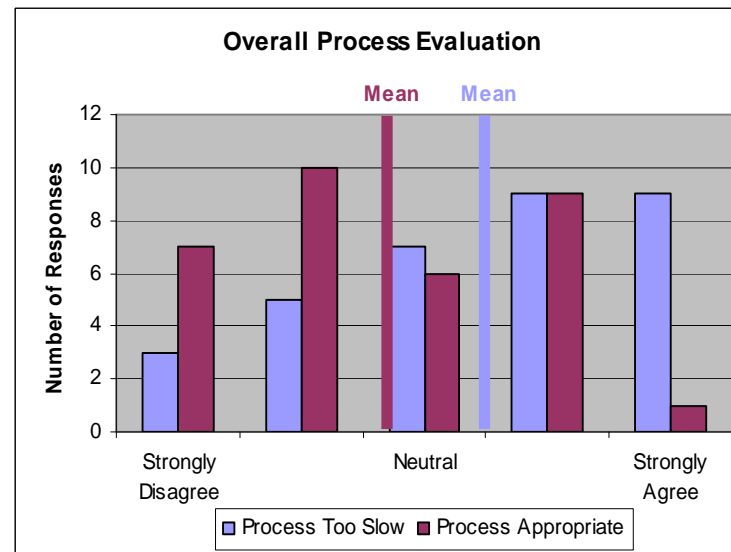
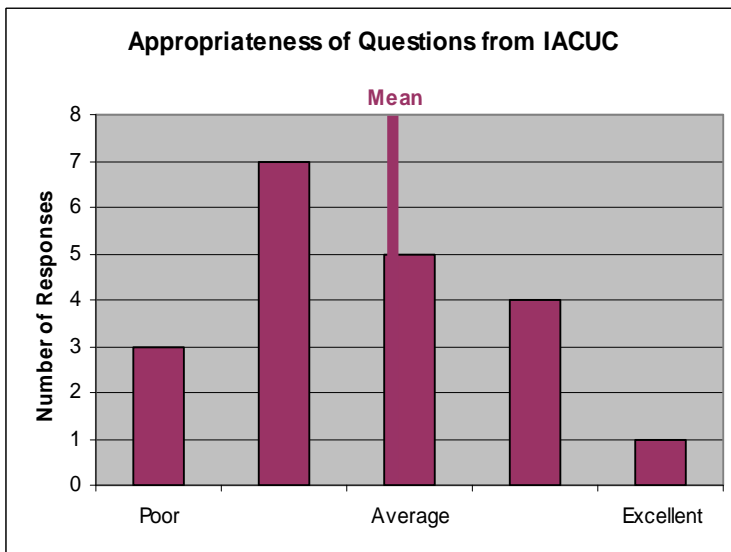
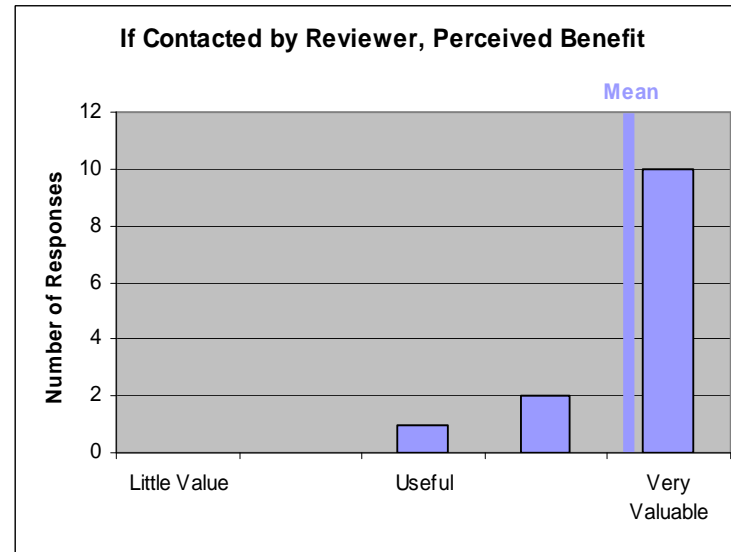
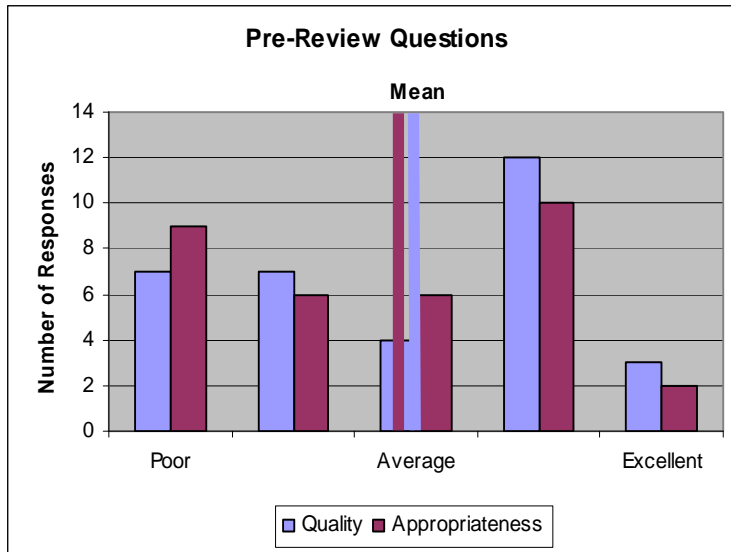


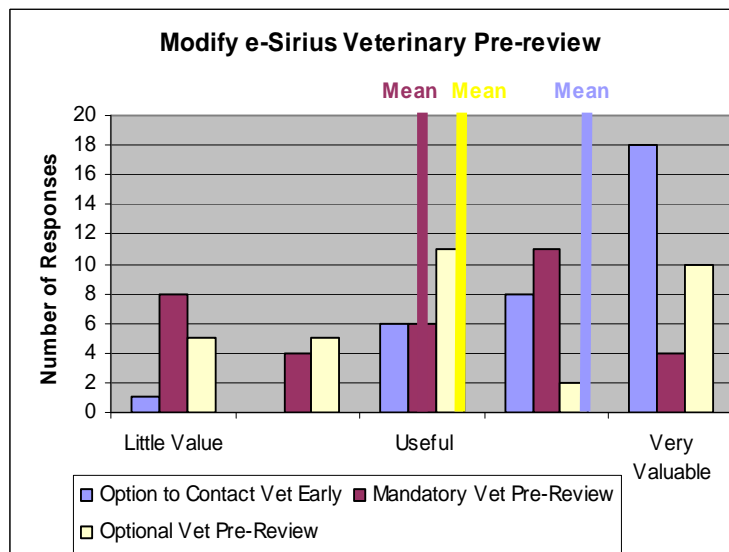
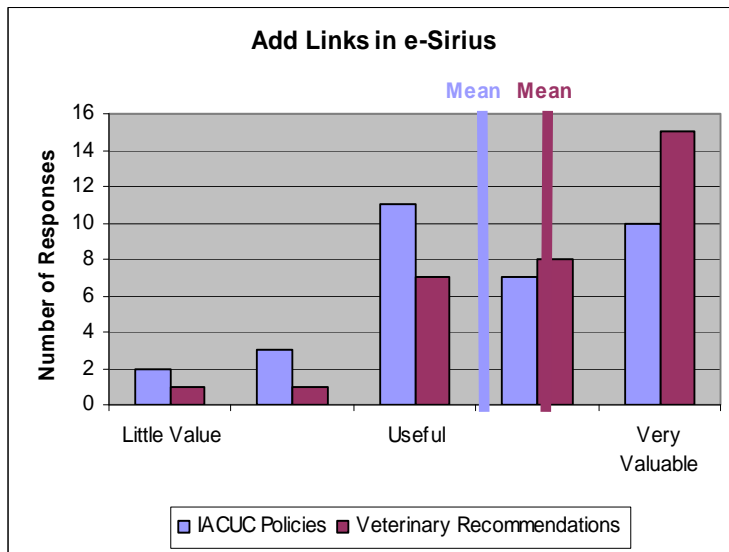
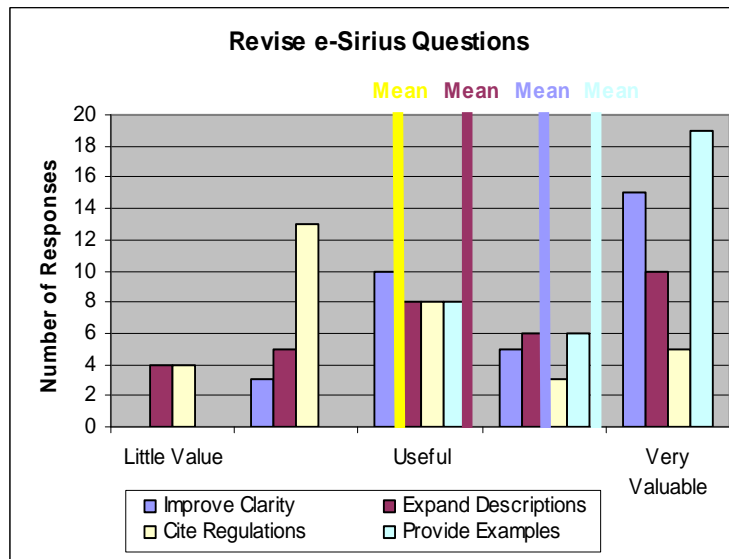
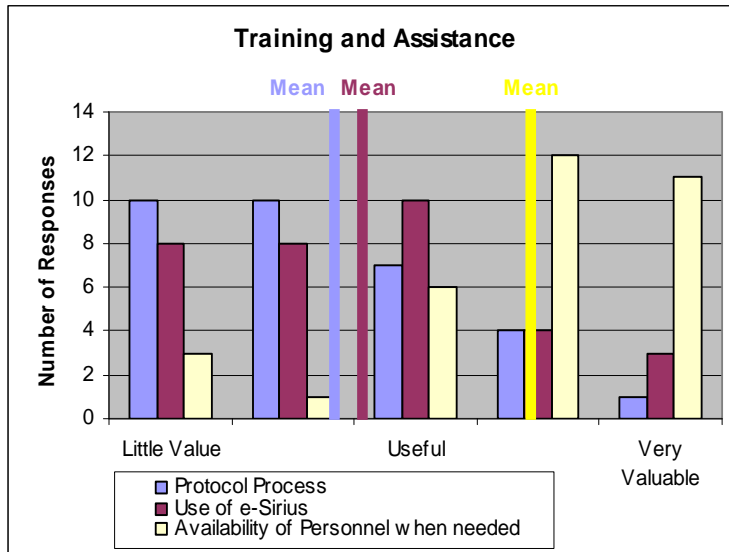
An empty rectangular text box with a thin black border. It contains no text. The box has a vertical scrollbar on the right side and a horizontal scrollbar at the bottom, indicating it is a scrollable area for text input.

Survey Results









Faculty Comments and Concerns (from the e-Sirius Survey – unedited)

If you have familiarity with a different animal use protocol system at another Institution, would you please provide some comments comparing the University of Kentucky e-Sirius system to the system at the other Institution. Comments addressing thoroughness of the questions, ease of protocol completion, review interactions, and approval time would be greatly appreciated.

- The best systems use pre-approved modules to facilitate the process. You can either accept the approved standard protocol or modify the standard with justification. The modified module must then be reviewed by the committee but protocols that do not vary from the norm are approved without the need for IACUC review.
- My colleagues at other universities where eSeries was been forced upon them hate it as much as we do. Our old Word-based protocols were much superior.
- e-Sirius is better than no system at all, as I would that that it helps the reviewer cover all IACUC guidelines. e-Sirius appears to unnecessarily burden both the PI and the reviewer with silly or confusing redundancies.
- e-Sirius is an improvement for the ordering of animals. It is a hindrance for the submission of IACUC protocols for review. Paper submission of protocols was more expedient for the investigator. e-Sirius has numerous problems with formatting errors, records deletion, form-fill issues, times where the system is off-line. Other institutions where I have worked had more slightly more direct and expedient IACUC approval processes. Review interactions were often expedited by invitation of the investigator to the IACUC meeting where his/her protocol was up for review. In this manner and reviewer questions that arose could be swiftly and succinctly addressed. This often expedited the approval process by a month or more.
- I have had multiple opportunities to look at the process at other institutions. Ours is, I believe, the most complicated and involved of any I have encountered. Our interpretation of the requirements by funding agencies and AAALAC appears to go beyond what is really required. The nature of the questions you asked, above, suggests to me that you don't appreciate the nature of the real problem: our "system" is significantly more stringent than is actually necessary. I understand that e-Sirius may not be the best system that could have been adopted, but that is NOT the real problem. The vets come back with requests for details that are NOT necessary - I base this upon my many opportunities to see what information is required at other institutions, not on what I happen to think is required (or maybe even what I know from some familiarity with the regulations).
- I have been on an IACUC committee at two different institutions before I moved to UK. This is the most cumbersome and time consuming system I have seen. At the last place I was we had forms that were developed by the University itself

and that was submitted by e-mail and routed electronically. eSirius is a terrible program because you can not navigate easily between the different sections and you can not copy/paste between one protocol and another in an easy fashion. You end up doing a lot of senseless double or triple work. The biggest problem with the review process is the time from submission to approval. At the other two institutions there was no prereview and that is what takes so long here. The protocol can go back and forth 4 or 5 times which wastes a lot of time. This process has to change.

- I can compare e-Sirius to the way it was before e-Sirius. I find the process through e-Sirius to be extremely cumbersome. What used to be a 15-20 page document is now a pdf with 80-100 pages. The only way to go through this and not lose track of what is there, where it is, what is missing and where the repeats might be is to make a word document, answer questions in the document, then cut and paste into e-Sirius. Time saver it is not, at least not the people writing the protocol. Now, for the reviewers, how is it?
- I have worked at and submitted IACUC protocols at two other major (larger/higher ranked) institutions. In both cases, there was a document/form that was filled out and emailed in. A document of questions was emailed back for response and your protocol and response to the questions is what went before the whole committee. I had the model IACUC proposal at one of these institutions, one that was posted as the example everyone should follow. However, upon submitting this same information to the UK IACUC, it was not enough and it took me months to get approval to work with animals. At both of these other institutions, if you had a protocol that was previously approved, this made subsequently submitted (and similar) protocols easy to get approved. You really only had to go through the worst scrutiny one time and once you got your protocol and methods where they should be, the IACUC trusted prior IACUC committees to have fairly reviewed the protocol. You could cite that methods were identical to X approved protocol and it seemed to reduce the workload for both sides. Here it is clear that each protocol is strictly considered individually, even when your methods are the same, but perhaps something as simple as the age of your animals is different.
- I have worked with many types of protocol submission form from paper submissions to electronic submissions under a system called Granite but in my many years in research, I have never encountered such a useless waste of time and resources.
- The eSirius system is slow. The questions are not organized in a logical manner and going back to find specific sections is not always straightforward.

Other comments or recommendations would be greatly appreciated:

- Consistency amongst the veterinary staff is key. This is not always the case. For example, during an annual review of my protocol I was asked to add a specific drug in the Surgical Procedure Section and then be told to remove it (because of little value) during the 3-year re-write review of the same protocol using the same surgical procedures. Now, the review process is anonymous, but I suspect that 2 different veterinarians made those very different comments. I understand that

there is turnover, but there veterinarians and scientific reviewer should be instructed to review as per similar guidelines.

- Please make esirius more user friendly. It is awful!!
- During continuation reviews, reviewers often raise issues about procedures that have been previously approved. This should not be allowed. Overall the process takes many times longer than it did in the past with no apparent benefit.
- The Esirius site itself causes much of the confusion. I have had portions of my application "disappear" on reviewer screens, have been asked to modify portions of a proposal but been locked on of editing information of the screen, and other glitches that make the process more difficult than necessary. Indeed, my first proposal was a very simple breeding request, that expanded to over 20 pages and despite my best efforts at compliance was not approved until one of the vets came to my office and spelled out the changes that were needed. Since then I have passed all of my proposals by the same vet-and have not had any serious problems. The ability to talk on the phone with him has eliminated any issues with my ability to respond in a manner that addresses to his comments. However, this might not be fair to the vet. This is very similar to the process prior to eSirius that worked well. If example protocols could be provided on the eSirius site that would be very useful. Often the questions that arise are simply overlooking issues that the IACUC committee requires rather than any disagreement about the appropriates of the proposed studies. The inclusion of "approved" modules of standard animal procedures would greatly simplify the process for both individual labs but also members of the IACUC panel.
- The IACUC staff are helpful but clearly are very very busy. What happened to Judy Tucker? She was extremely helpful and friendly. eSerius is unnecessarily cumbersome, time consuming, and confusing; it adds no value to animal care and use. Ditch it. In the 7th question re whom we contacted for help? Why won't this form let you choose more than one answer, ie, IACUC staff, DLAR vets, AND other colleagues? This is indicative of computer-based forms that ask for specific information and then won't let you provide that information.
- I had such a horrible experience with trying to give the vet reviewer what they wanted through a LARGE number of resubmissions that I am extremely reluctant to submit any protocols in the future that involve anything more than sacrificing animals for tissues. In fact, there are some disease-related proof-of-principle animal studies I think would be very important and exciting for us to do that relate to our current projects, but I am extremely reluctant to propose them because of the very painful experiences I have had in the past.
- Personnel section of e-Sirius is time-consuming and in large part unnecessary waste of time -- too many boxes to check. e-Sirius questions seem redundant.
- Overall, the IACUC often vastly oversteps the bounds of what their authority and governance should be. The IACUC, for any institution, should be concerned with one question above all others, is animal research conducted in a humane manner. Other than the welfare of the animals, the IACUC should not have any concerns or authority over the quality of the research being conducted. The

quality of the research, its significance, overlap with already existing studies, etc. are all the provenance of grant review and peer-review processes for publication. In short, mechanisms to control the quality of science undertaken are already in place. Bad science doesn't get funded and it doesn't get published. Two fundamental changes could be enacted to make the IACUC process at the University of Kentucky more stream-lined and effective. The first would be to revise the IACUC forms to reduce or remove the burden on the investigator from having to explain the background, significance, and methodology of his/her research. The second would be to train IACUC reviewers to target their responses and questions solely to the welfare of animals involved in the studies proposed.

- My colleagues and I feel that it would be very beneficial to have certain aspects of protocols that are very common to be put together in a format that is updated regularly by the staff, that could be accessed, modified, and pasted into our protocols. I feel like I am reinventing the wheel when I describe details of procedures that are very common, and then defending them and doing searches, etc. If some of this could be "boiler plated" so that we could paste in the pertinent details, the system would be much easier. thanks
- Several years ago the veterinarians were almost universally regarded as the "PI's friend." When they visited a laboratory you knew you were going to get some help. The comments on preliminary reviews of the protocols were certainly intended to make sure we adhered to the requirements, but they also were perceived as resulting in better, more reliable experiments. I am afraid that is no longer the case. The level of details the vets (I assume it's the vets, not the faculty reviewers) require is unnecessary, obstructionist, and does not result in improved studies. I appreciate greatly that we must not be found out-of-compliance, and any such instances must be corrected, but the present system goes far beyond this goal. The investment of time required to perform the now-onerous task of submitting protocols is unacceptable. I hate to write so negatively, but this system needs to be re-configured. The most important goal must be to reestablish trust and collegiality between the DLAR veterinarians and the investigators.
- The major problems with e-sirius is the redundancy and the number of screens to go through. Also, it is not clear where specific items (usually attachments) should be placed - in many cases I had the information wanted, but the reviewer was looking for it in a different place. I think the anonymous electronic nature is adding extra work to all involved - ideas and suggestions are best understood with direct human to human contact. PIs and/or delegated lab staff should have the opportunity to attend the review to fully understand concerns of IACUC (as in the IRB process). Having an individual pre-review the protocol openly (not anonymously) and adding SOPs or examples would also facilitate the process.
- I found the e-sirius system very complicated in the beginning, but have learned it now, and it does not take as long to complete as I expect. Jill Esham has been incredibly helpful and up-beat -- which has probably been extremely challenging, as no doubt she has had to deal with lots of disgruntled PIs. The time for having an application processed has also greatly decreased; I really appreciate this! The pre-review by IACUC staff for administrative/procedural issues is also helpful. A

- year ago I would have paid a lot of money to have the e-sirius system discarded, but am starting to think that perhaps the system can work.
- As I see it, there are three major issues with the eSirius process. First, eSirius reviewers should maintain a narrow focus on issues directly related to animal care and use, and refrain from other comments on experimental design, etc. Along the same lines, the IACUC should neither request nor have access to a complete copy of any grant or grant application- an appropriately filled out eSirius form should provide the committee with all of the animal care and welfare relevant information needed. Second, the demand on PIs to research and defend methods for killing animals seems the least efficient use of resources. The PI is far less qualified than vet staff regarding appropriate application of euthanization protocols. Instead, it would be much more helpful if the vet staff provided a set of approved protocols that they reviewed and updated yearly, and eSirius used a drop down menu. Researchers could then click on the approved method and all details and justifications would be established. Vets could also provide some sort of training/certification for approved protocols (as are provided for chemical hygiene and hazardous waste). If an experimenter has some unusual method, then provide an 'other' category to allow that investigator to defend their own protocol. Third, the byzantine and awkward nature of the eSirius application process is off-putting and difficult to follow. Highly redundant information is requested in multiple areas and it is nearly impossible to navigate back and forth between sections to copy and paste relevant text without losing work. In addition, after completing the application, the printable version is incredibly long and very awkwardly formatted- it is nearly useless for maintaining a hard copy file of the application. Final comments: The IACUC at UK has been/ is perceived by many PIs as a 'petty tyrant' insisting that PIs dance to its tune in order to receive the approval needed to initiate animal experiments. True or not, this perception needs to be corrected. Given the current funding climate, researchers need help achieving their research and funding goals, not further impediments. Perhaps some sort of PR campaign is in order. We don't need a mandatory pre-screening from Vets on the IACUC application, its first round review includes veterinary input already. However, we might be able to use Vet input on the parent grant. Another concern is that it is rumored that some members of the IACUC may be financially involved with eSirius. While it makes perfect sense that someone involved in an IACUC would be in an ideal position to see the need for a system like eSirius, it creates a conflict of interest. If there are members of the IACUC who maintain financial ties to eSirius, those relationships should be clearly posted on an IACUC website and advertised to PIs. Further, those members with financial ties should recuse themselves from evaluation of eSirius.
 - I wrote my protocol on eSirius about 2 years ago, and things may have improved since then, but here are/were my basic complaints. Poor interface. I think you all should look at NSF's FastLane software, and how it integrates its various sections seamlessly into pdf files that can be proof read before final submission. When I submitted my IACUC proposal on eSirius, I never knew what the finished product that reviewers read would actually look like. Hopefully, they didn't have to read the same awful web interface that I did. NSF's FastLane, by contrast, takes word documents, pdf documents, or text cut and paste into their fields, and generates "proofreadable," reviewable pdfs from that, one section at a time, or

the whole thing at once. It's so much easier to navigate. It takes way too long between initial submission and approval. I don't recall if there was a separate preliminary review, but my proposal took two rounds of review and over 3 months to get passed by IACUC, after more than 20 years of getting proposals accepted after one round (plus some hints from Ken Dickey). The entire process takes too long. The first set of reviewer comments was several pages longer than my proposal itself, and my proposal had been modeled on a format that IACUC had accepted for ~20 years. Obviously, there is always going to be a learning curve as new regulations are put in place, but this was excessive.

- provide boiler plate templates for standard protocols would make the process less burdensome.
- This survey appears to worry a bit too much about approval time. From my experience, time is not a problem, what is a problem is the relevance of the reviewer's comments to animal welfare. Many a time, I have received reviews that did not deal with animal welfare at all (admittedly, this problem improved substantially during my second submission through e-Sirius). Another problem, is the inability to address the reviewer's comments directly inside of e-Sirius in an empty box like the one I am currently typing in. Instead, one is forced to accept the reviewers points and make modifications to the protocol itself (completely preventing open communications between the author and the reviewer). I have to admit that the second submission was about 100% easier than the first time around. As long as the pre-populated fields are there for everyone to choose from and not just for me (based on my prior IACUC), then I can see the improvements. This survey, I hope, should be compared to the surveys taken the first year e-Sirius was put in place.
- There needs to be a separate format for teaching protocols that are not associated with research projects.
- Item 4 and 5 just above - My answer really depends on familiarity with the system and who you get as the reviewer. I don't like doing things twice. I like to do things well once so as long as it doesn't place any additional time/work burdens on me, fine. My comments will reveal my identity, I fear. I hope efforts will be taken to protect my work from repercussions. eSirius needs a "save" button. Specifically, I need to be able to save a page while I am working on it, not go to the next page, not quit but just "save". I cannot tell you the number of times the browser has locked up or something has happened and I have had to start all over on a page. This is horrendous when it happens on the search for duplication page (this just happened to me this week!). I am still really annoyed at the personnel section. This is another example of how something simple has been made ridiculously cumbersome. If I am adding a person to the protocol, I am adding them to perform everything. There needs to be a "full add" button so that I do not have to go through and select every single methodology that the person performs. My biggest complaint is the inconsistency and perhaps unfairness in the review process. I am happy to provide additional information when it is left off or clarifications. However, I am shocked at the number of methods (even though consistent with "The Guide") that one particular reviewer has decided just should not happen on this campus. It has been made clear to me by my colleagues that I have unluckily had the one reviewer who is clearly "anti animal research."

According to my more senior colleagues, I have had the worst possible experiences and one reviewer has made it so bad that it seemed that my animal research was not welcome here in Kentucky. Some examples that have occurred:

- Reviews are inconsistent for what is essentially an identical useage method across my 3 protocols. (I copy and paste when at all possible so reviewers are getting the same info). I have to fight to keep the protocols consistent in methods because I know we won't remember to do one thing on A protocol but another on B protocol. I have gotten some fair and appropriate reviews but I have one reviewer who clearly does not want my type of work to occur on this campus. This has forced me to create ridiculously detailed protocols (though I now have other reviewers impressed by the extent of detail and organization).
- It is inappropriate and definitely inconsistent if the interpretation of pain and distress levels rank getting a rat drunk higher than chopping off the rat's head. I am as yet unaware of any measure that indicates "distress" in an ethanol-intoxicated rat. In fact, I would argue that an ethanol-intoxicated rat (that is not allowed to withdraw) is in less distress than control rats. I have not publicly fought this battle yet but my alcohol research colleagues are all in agreement on this point. This is inconsistent with opinion of IACUCs across the country as well.
- Lack of knowledge or awareness of what is acceptable in "The Guide" or general practices across the country. For example, it is inappropriate that I have been asked to administer anesthesia to withdraw blood when my rat is at nearly surgical plane anesthesia due to alcohol intoxication. The blood draw procedure was consistent with "The Guide" and I was citing a standard operating procedure of the IACUC of a major institution (larger and more highly ranked for that matter). Sure, it should be evaluated but to not even consider a larger/better school's IACUC opinion is ridiculous. To ignore or overrule the PI statement that a method has been performed for 8 years successfully without any pain or distress should not happen.
- It is inappropriate that various sections of my protocols have consistently been deemed unacceptable when theses sections were written with the study director for the Committee on Guidelines for the Use of Animals in Neuroscience and Behavioral Research at the National Academies. If anyone knows what is acceptable verbiage for animal use, it is she. Further, she ran IACUC 101 workshops across the country, yet the sections were not acceptable to UK? (really, it was just the one reviewer)
- Peer reviewed scientific articles should be acceptable support and take precedence over the personal feelings (i.e. not scientifically supported) of a reviewer. I remain puzzled how six pages of citations of peer-reviewed articles were not strong enough to support and justify why I chose to perform a method in a particular way. This was most disturbing because I cited another paper that directly showed that stress hormones were not altered by my proposed procedure. What better support is there for a method? That method, incidentally, was also consistent with "The Guide" but that did not matter to the reviewer either.
- Decapitation as a means to obtain brain tissue for certain assays ranks as Level D for some reviewers and Level E for others. This needs to be consistent. This drives me nuts because inevitably it is always the opposite one from what I put in the protocol.
- The protocols are requiring too great of detail, which burdens both the reviewer and the researchers. Specifically, there should be some flexibility allowed in sacrifice timepoints (but not humane endpoints), blood withdraw timepoints and other experimental manipulations that really do not impact animal well being. For example, what if I want to sacrifice my rat at 26 hours after the last dose but my protocol says 24? I have been forced to

be very specific when I really think I should be able to say that animals will be killed in timecourse or at timepoints consistent with experimental questions. Perhaps merely give a range of survival timepoints (2 hours to 2 months?). In a perfect world, I would like to state that I have X level C, Y level D and Z level E rats that will be used. With description and justification of each level, that should be enough information for an IACUC. • An easily accessible site or standard operating procedures library for common animal use items. That way, we know how things are to be performed and we can write them appropriately. In many cases, I just need to know how the committee wants something done and/or written in the protocol. In other words, just tell me how to do it and I/we will. • Reviewers should not be critiquing the science behind the protocol. They should restrict comments to animal use. The moving target aspect of these reviews is completely frustrating. These difficulties create such an adversarial environment that PIs just ignore requirements and do what they know to be correct and humane by the normal person's interpretation of "The Guide." I have expressed to various "powers that be" that making this protocol system difficult and cumbersome merely promotes a noncompliant environment. Can you believe that senior faculty have told me to just write whatever it is that the reviewer wants, but to just do whatever I want to do? I don't function like that and I will continue to fight to create a system that works for both sides. And kudos to Dr. Jeff Smiley for his common sense approach and ability to find solutions when I was about ready to move my \$2million program to an institution that works WITH animal researchers and not against.

- This user finds the protocol application system and submission of amendments unnecessarily cumbersome. It seems as though the e-Sirius system was created to make the IACUC staff's job easier at the expense of the time and effort of applicants.
- It has improved over the few years it is in use. Most helpful would be acceptable methods, procedures that investigators can plug into their application, so we don't have to guess at what is acceptable to the IACUC. I do not see why the reviewers are anonymous. I tried to ascertain the identity of the veterinarian reviewer a few years ago and was denied that information. This is not an example of transparency
- The esirius protocol submission form is cumbersome, unforgiving, and redundant. It requests or requires useless information and then does not allow you to provide it in a logical order. When you finally DO manage to provide the information, the IACUC questions even the simplest of procedures. The esirius submission was touted as the ultimate in protocol submission. My question is, if it is so wonderful why doesn't it work? Every time you turn around it is down for maintenance or down for upgrade or down for backup or down for the hell of it. Are the people who are supposed to maintain this state of the art system incompetent or do they just bring the system down because they can. It seems the only people who benefit from the electronic submission are the people who sold you this white elephant.
- The specific information required in each section is not well-defined. In particular, those sections relating to the actual procedures to be used seem to be redundant. In fact, on two successive protocol submissions (one month apart)

that used identical procedures (which also seems silly, by the way), I was asked by the IACUC to cut and paste information that was approved in one protocol into a different box for the second protocol. Also, if specific wording is required by the reviewer or committee, I suggest the protocol be directly edited by the reviewer and a note made for the PI to see edits rather than writing out what needs to be changed and then asking the PI to copy and paste the comments into the appropriate section.