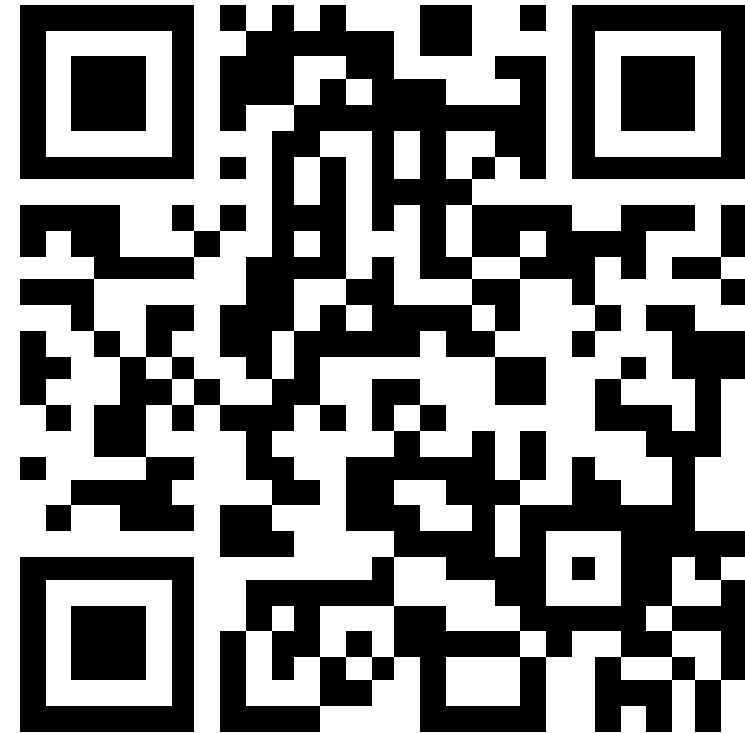


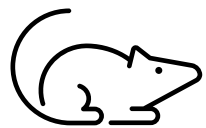
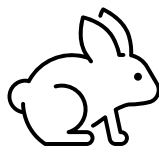
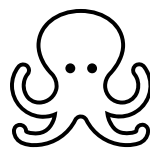
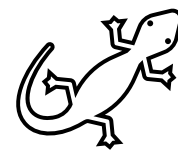
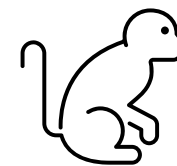
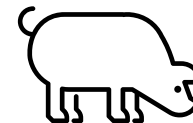
<https://app.sli.do/event/wH55XPAq3LQVtYq5fucNaK/live/questions>

Please register your
attendance outside
the auditorium



Submit anonymous
questions to IACUC





IACUC TOWNHALL

29 AUG 2024
CELS AUDITORIUM

AGENDA

- ❑ Opening address by A/P Sanjay Khanna, IACUC Chair
- ❑ Presentation by IACUC Office
 - ❑ Protocol review timeline
 - ❑ Non-compliances
- ❑ Presentation by Dr Leslie Retnam,
Attending Veterinarian,
Director, Comparative Medicine
- ❑ Q&A
- ❑ Closing Remarks by IACUC Chair



DR MOHD ZACKY
COMPLIANCE OFFICER

PROTOCOL REVIEW

PROTOCOL REVIEW

The use of animals for scientific research is legal bound. – Animals and Birds Act (1965) – Care and Use of Animals for Scientific Purposes Rules (2004) – NACLAR Guidelines, 2022 (AVS)

It is imperative that the constitutional requirements are met.

Rules:

(2) An institutional animal care and use committee shall not grant its approval for a proposed project or for any significant change to an ongoing project unless the committee is satisfied, upon conducting a review of the components of the project, that the care and use of the animal will comply with the following requirements:

NACLAR Guidelines:

II.11.2 IACUC approval

II.11.2.1 Before any protocol begins, PIs must submit a proposal to the IACUC.

II.11.2.2 PIs, and those working on their protocol, must not begin work on a protocol or amendments to a protocol before written IACUC approval is obtained, and must adhere to the approved protocol and any requirements of the IACUC.

PROTOCOL REVIEW PROCESS



Submission ≠ Approval

Submission deadline e.g. For Jul review

Day 0

- Same day as the IACUC meeting to review the previous month application e.g. Jun
- Generally, falls on the **3rd Monday of every month**

Administrative review and clarifications by IACUC office

Week 1

- PI reply time usually short if submitted close to deadline
- **Review deferred** e.g. a) incomplete submission, b) breeding without research applications

Joint Office meeting and clarifications (JOM)

Week 1-3

- **Week 1-2:** Review by vets. CM Ops. CMIF, ORMC
- **Week 3:** Premeeting clarifications by PI. **Note:** PI reply time usually short (3 working days or 5 days including weekends)
- Review of poorly written or big complicated applications might be deferred

IACUC quorate review

Week 4

- Review by Designated IACUC members (DRs)
- Minor concerns to be addressed by post-meeting clarifications
- Resubmission might be needed e.g. a) poorly written, b) animal welfare concerns, c) biosecurity issues e.g. bringing live animals out of vivarium for procedures

Postmeeting clarifications and approval

- Approval **after** - a) DRs accepted PI post-meeting clarifications, b) OH enrolled, c) RCULA training completed d) ORMC approved, e) IRB approved if human cells or tissues used, f) BMT passed

AVOIDING DELAYS

IACUC Office has received numerous feedback on protocol approval delays. Delays can arise from reviewers or PIs, or both.

- ✍ Reviewers do not have the same experience or background as Applicant, use lay language for easy understanding. This would also be helpful for the non-scientist reviewers
- ✍ Missing information – what is obvious to researcher, might not be to reviewers
- ✍ Reviewers do not have the familiarity of running the experiments, step by step description is crucial
- ✍ Avoid large protocols (e.g. protocols with numerous strains and experiments)– difficult to review, large volume of information, higher chances of errors

TIPS FOR AVOIDING DELAYS

Clarity

- Experimental timeline can be long and multi-stepped
- Provide headings to break down full procedure
- Instead of a descriptive paragraph, describe sequence of events in a timeline fashion
 - 1) 7-8 weeks old mice will be exposed to open field apparatus for 30mins (refer to Procedure B section 1.9 for details on open field apparatus).
 - 2) 3 days after open field exposure, mice will be injected with R2D2 (route, volume) (refer to Procedure A for details of stereotaxic injection)
 - 3) 14 days after R2D2 injection, mice will be exposed to elevated plus maze for 30mins (refer to Procedure B section 1.9 for details on elevated plus maze).
 - 4) Mice will be euthanized on the same day after elevated plus maze experiment.
- Surgical and non-surgical procedures should be described in full (Procedure A, Proc B1.11)
 - Preparation, pre-emptive and post-operative drugs, aseptic techniques

TIPS FOR AVOIDING DELAYS

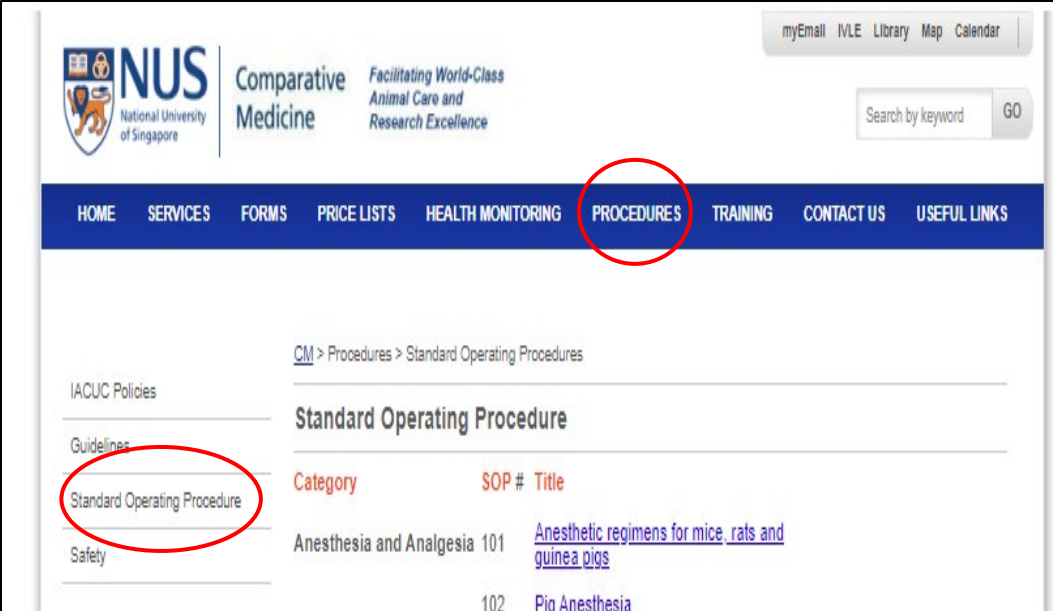
Consistency

- Application form has multiple sections with repeated information
 - Section 5.2/5.3 = Procedure A = Procedure B
 - Section 2.1 = Section 2.2 = Procedure A
- Inconsistencies between sections
- Dose, volume, route, and frequency of administration
- Frequency of procedures e.g. blood collection, imaging
- Method of anaesthesia, euthanasia
- 'Referring' method to mitigate inconsistencies

TIPS FOR AVOIDING DELAYS

Compliance

- Refer to CM SOPs for information on standardized information
- Anaesthesia, euthanasia, post-surgical care, pre-surgical preparation
- <https://cm.nus.edu.sg/standard-operating-procedure.php>
- Provide justification if not able to follow the SOPs



The screenshot displays the NUS Comparative Medicine website. The top navigation bar includes links for HOME, SERVICES, FORMS, PRICE LISTS, HEALTH MONITORING, PROCEDURES (circled in red), TRAINING, CONTACT US, and USEFUL LINKS. The left sidebar contains links for IACUC Policies, Guidelines, Standard Operating Procedure (circled in red), and Safety. The main content area shows the breadcrumb trail: CM > Procedures > Standard Operating Procedures. Below this, the title 'Standard Operating Procedure' is displayed. A table lists SOPs with columns for Category, SOP #, and Title.

Category	SOP #	Title
Anesthesia and Analgesia	101	Anesthetic regimens for mice, rats and guinea pigs
	102	Pig Anesthesia

TIPS FOR AVOIDING DELAYS

Consult

- Approach IACUC Office if you need help with new submissions or renewal protocols, CM for veterinary consults
- Check with the IACUC Officer handling your protocol for amendments
- Drop an email at dprbox33@nus.edu.sg (IACUC General enquiries)
- Submit earlier for sufficient time for pre-screening

AFTER APPROVAL

Finally, the protocol is approved. What next?

- ✓ Latest version of the approved protocol made available in the laboratory
- ✓ Ensure that each member of the research team listed in the protocol is familiar with the content of the protocol e.g. experiments; doses, routes, frequency, of administered agents, monitoring frequency, humane endpoints
- Lack of familiarity with protocol stipulations can lead to non-compliances.



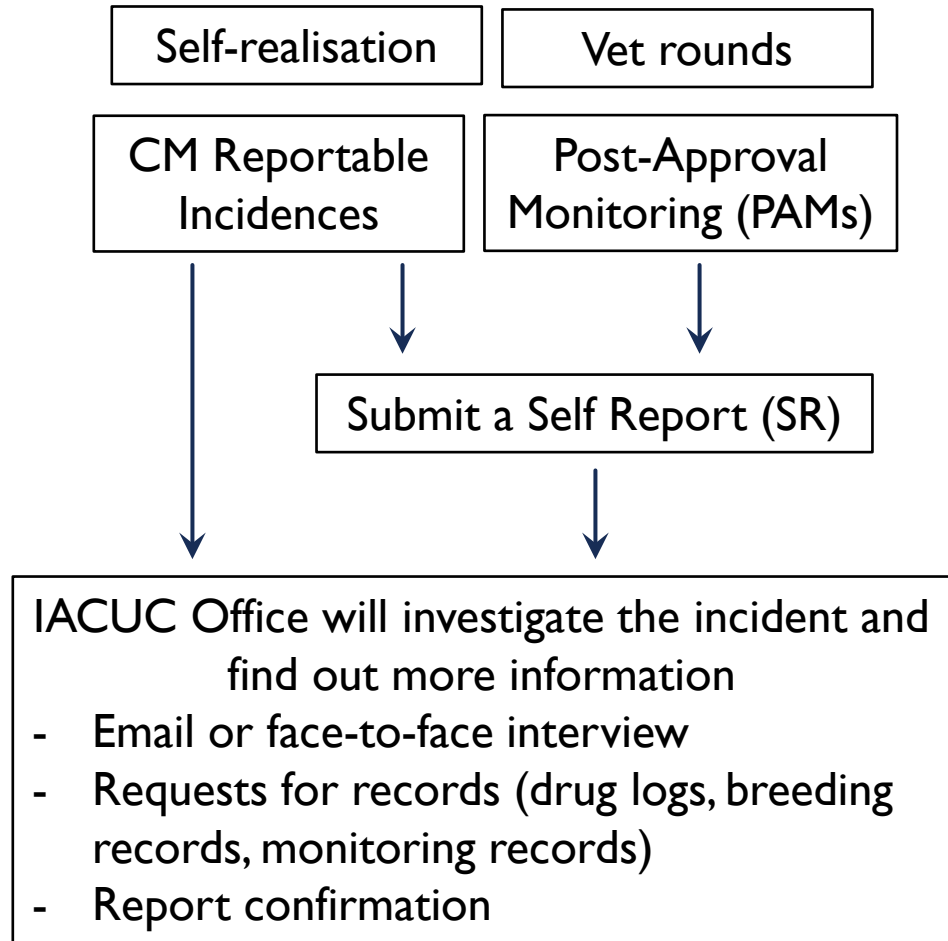
COMMON NON-COMPLIANCES

WHAT ARE NON-COMPLIANCES?

- I Deviations from the IACUC approved protocol
 - e.g. when performing a procedure incorrectly, not monitoring animals post-procedure, administration of agents via wrong route
- II Performing a procedure NOT in the approved protocol or prior to IACUC's approval
- III Unapproved personnel performing an approved procedure

The stipulations in the protocols **must** be adhered to **exactly**.

DETECTING NON-COMPLIANCES



III.6.7.7 Some examples of sanctions include:

NACLAR Guidelines (2022)

- letters of reprimand;
- mandating specific training aimed at preventing future incidents;
- monitoring by the IACUC or IACUC-appointed individuals of research, testing, or training involving animals;
- temporary revocation of privileges to provide animal care or to conduct research, testing, or training that involves animals, pending compliance with specific, IACUC-mandated conditions;
- permanent revocation of privileges to provide animal care or to conduct research, testing, or training that involves animals; and
- recommending to the IO that institutional sanctions be imposed.

Presentation
to IACUC

Outcome

COMMON NON-COMPLIANCES

For Self-Reports

2022 = 13

2023 = 11

2024 (Aug) = 20

Of the 20 SRs

Deviations = 5

Unapproved strain = 1

Unapproved procedure = 5

Wrong technique = 2

Monitoring = 3

Breeding configuration = 1

Post-op care = 1

Unclassified = 2

- ✗ Deviations from approved protocols
- ✗ Performing unapproved procedures
- ✗ Unauthorised entry into vivarium
- ✗ Failure to euthanise in a timely manner
- ✗ Unapproved breeding configuration
- ✗ Breeding unapproved strains
- ✗ Failure to provide pre-emptive or post-operative care
- ✗ Failure to complete post-operative regimen
- ✗ Not keeping proper records
- ✗ Not monitoring according to stipulated frequency
- ✗ Not maintaining aseptic techniques in surgery
- ✗ Wrong procedural technique

RATIONALE

- Wrong technique can jeopardise animal welfare
 - Spraying the mouse into alcohol to sanitize injection site > potential hypothermia, shivering > distress
- Failure to monitor animals at the stipulated frequency
 - Objective is to monitor the condition of the animal before and after procedure
 - Capture the moment humane endpoint is reached for intervention and/or timely euthanasia needed
 - Do not cause unnecessary distress by delaying euthanasia till moribund
- Administering unapproved agents (cell lines, drugs, ...)
 - The potential adverse effects on the animals must be considered before approval is given
 - Untested agents pose a strong biosecurity risk to **ALL** animals in the vivarium and their users

RATIONALE

- Unapproved breeding configuration
Overcrowding > trampling > animal death (wasted crosses, pups)
- Failure to complete post-operative regimen
Animals remain in pain and distress during recovery, potential infections
- Unapproved experiments
Jeopardising animal welfare
Approved experiments under the wrong protocol = non-compliance
Protocol adherence from submission of animal order till euthanasia

GOOD WELFARE = GOOD SCIENCE

 **frontiers**
in Behavioral Neuroscience

OPINION
published: 30 November 2021
doi: 10.3389/fnbeh.2021.763428



Review > Lab Anim. 1997 Apr;31(2):116-24. doi: 10.1258/002367797780600198.

Happy animals make good science



T Poole ¹

Affiliations + expand

PMID: 9175008 DOI: 10.1258/002367797780600198

Combining Animal Welfare With Experimental Rigor to Improve Reproducibility in Behavioral Neuroscience

Cássio Morais Loss^{1,2*}, Fernanda
Cilene Lino-de-Oliveira^{5†} and

PERSPECTIVE

Focus on Reproducibility

Improving quality of science through better animal welfare: the NC3Rs strategy

Mark J Prescott & Katie Lidster

Edited by Jennifer Sills

Good science requires better animal welfare

Biomedical research suffers from a crisis of reproducibility and translatability (1), with some studies estimating that more than

TAKE-HOME MESSAGES

- I Begin work only after protocol/amendment is approved by the IACUC.
- II Approved protocol **must be exactly** adhered to. Otherwise, it becomes a non-compliance.
- III All aspects of the experiment must be approved by the IACUC prior. Submission $\neq$ Approval
- IV Stipulations in approved protocol are in place to ensure animal welfare is not jeopardised.
- V Good animal welfare makes good science.

DR LESLIE RETNAM

DR ILONKA GUENTHER

MR WONG SHEE WING

MS SYLVIA YEO

COMPARATIVE MEDICINE (CM)

PARTNERING WITH CM
FOR YOUR ANIMAL RESEARCH NEEDS



Q & A

EARLY SUBMISSIONS

My lab is working on the early adaptive immune system in white-spotted bamboo sharks and assisted reproductive technology for sharks and rays. Now we purchase sharks from Jurong fish port or Little India wet market, or obtain shark and ray sperms from aquarium. I wonder if we can apply for license on performing experiments on sharks and shark cells.

If shark/ray tissues are purchased for in vitro use only, please contact ORMC to ensure that all safety requirements are met.

If they are intended for in vivo experiments or procedures in live animal models, please submit an amendment to your existing protocol or submit a new application for prior approval.

EARLY SUBMISSIONS

How does IACUC help Singapore and NUS maintain international excellence in preclinical research, esp. through a swift approval process?

- The IACUC also has the responsibility to abide by Singapore's law and statutes.
- Its key responsibility is to ensure that animal welfare is not jeopardised.

EARLY SUBMISSIONS

We have not received any comments since we submitted the application in April. Why does it take so long?

Why does it take years to approve a new location for mouse sacrifice? What is the bottleneck here and why no flexibility granted to researchers?

How is IACUC ensuring unbiased recommendations, independent of CM's financial interest to markup resources/services? What is helping avoid conflict of interest?

We request that this PI/Researcher write to IACUC (dprbox33@nus.edu.sg) and provide details for IACUC to look into the matter.

EARLY SUBMISSIONS

Does the IACUC think a 160-character limit is critical for getting valuable feedback and questions during town halls? 😊 It seems quite difficult to pose Qs

- Use of an online platform was to provide anonymity (if necessary). Character limitation is a system's limitation.
- Alternatively, concerns or feedbacks can be directed to dprbox33@nus.edu.sg.

EARLY SUBMISSIONS

Protocol library

- Due to confidentiality, protocols cannot be shared. However, that would be an idea worth exploring if PIs are open to sharing their protocol.
- Office is currently drafting a document that would provide template responses as well as points to note when completing the iORC forms.
- Please note that no two protocols will exactly be the same, so the broad use of libraries needs to be selective.

EARLY SUBMISSIONS

Protocol delays

There is a set time of 2 weeks for reviewers to respond. However, due to exigencies of duties, reviewers may take more than 2 weeks to reply. A reminder system is in place to encourage reviewers to reply.

There are ongoing changes in the review process – workflow, manpower - to make the process smoother and more efficient for all stakeholders.

Protocol delays can be attributed to reviewers, researchers, or both. IACUC Office is open to meeting with researchers to craft out applications before submitting for review. PIs should also play a part in screening the submissions.

EARLY SUBMISSIONS

Review process - Justifications

- Methods approved in previous protocols > PI must include past clarifications and conditions in the new applications for IACUC's review and consideration. Do not include reference statements e.g. 'as in protocol R19-1234'
- Every protocol is an independent document.
- Use of drug to compare with previous data/results from the lab is acceptable.
- Comparison with data from other laboratories (i.e. not from own lab) is reviewed on a case-by-case basis.
- Use of pharmaceutical grade agents and their conditioned exception is stipulated in the NACLAR guidelines (III.4.7 – Use of pharmaceutical-grade chemicals and other substances)

EARLY SUBMISSIONS

Review process – Quality of questions

- Efforts are in place to improve the quality of reviewers' questions, such that PI's response would not trigger more follow-up questions
- But this would require PI/Researchers to read the questions through and acknowledge the directions/comments given.
- Meeting with the reviewers is also an option to iron out the details.

EARLY SUBMISSIONS

Review process – Post-meeting

- A Word document- based post-meeting responses template went on trial for selected protocols for the August 2024 IACUC meeting.
- Feedback from reviewers is being gathered. Feedback from PIs who have received the post-meeting template are much appreciated
- IACUC Office is working on streamlining the workflow for both reviewers and PIs.
- PIs will be updated accordingly if there is a concrete change.

EARLY SUBMISSIONS

Feedback and effective changes

- IACUC takes feedback seriously. However, time is needed to gather concrete information to support the feedbacks and to determine if the feedbacks are not one-off incidences
- Changes have been and are being made to the review framework. We will continue to monitor the performance of the review process to determine if changes are effective.
- As mentioned earlier, protocols delays can arise from reviewers, PIs, or both.



LIVE Q & A

<https://app.sli.do/event/wH55XPAq3LQVtYq5fucNaK/live/questions>



Closing Remarks

Qualtrics survey



https://nus.sydney1.qualtrics.com/jfe/form/SV_7ZZxqiMRymeeQom

FEEDBACK
SURVEY