The Risk of Hazards, Hypothetically

Dr. Stesso Virale relocated to Great Eastern University (GEU) after working at Great Western University (GWU) for over ten years. Dr. Virale's research involves a line of transgenic mice that requires treatment with tamoxifen to activate a gene of interest.

Mr. Cooper, the GEU Post-Approval Monitor, decided to visit with Dr. Virale once his mouse colony and laboratory were established. During the visit, Cooper discovered that Virale was housing his tamoxifen-treated mice in a conventional housing room. Cooper informed Virale that the treated mice must be housed in containment, and, due to the potential non-compliance, a report must be made to the IACUC. Cooper also asked Virale to provide the safety officer with a list of staff members who were potentially exposed to the tamoxifen. Virale was invited to attend a GEU IACUC meeting to discuss the allegation of non-compliance. Before the IACUC meeting, the safety officer performed a risk assessment to identify lab and vivarium members' exposures levels and the impact the exposure could have had on their health. Upon completing the assessment, a notice was sent to individual staff and vivarium members informing them they may have been exposed to tamoxifen – via the handling of animals that were administered the chemical and/or cages that housed the animals – but that the levels of the chemical were so low that the risk was negligible. Virale also received this notice from the safety officer.

During the IACUC meeting, Virale explained that he uses tamoxifen in the animals' drinking water to turn on genes of interest in mice and that the dose he uses is negligible compared to the human therapeutic dose. He also explained that he was not required to house his animals in containment at GWU and apologized for the confusion. Once Virale completed his summary, GEU IACUC members engaged in discussion. One committee member reminded Virale of the importance in adhering to the safety officer's determination that tamoxifen use can pose a risk to animal users and must occur in containment, even if this decision is different from practices at GWU. Virale cited the notice he received from the safety officer, which indicated that the level of tamoxifen to which people were exposed was negligible and posed no risk. He asked the committee and safety team to explain the discrepancy between the policy and exposure notice, and why did his animals, that received such a low dose of tamoxifen, need to be housed in containment if the risk assessment indicated a negligible risk.

Should GEU revisit its policy on housing tamoxifen-treated mice in containment? Why or why not?

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A WORD FROM OLAW

In this scenario, the IACUC compliance monitor's understanding of the institution's policy on the containment of tamoxifen, a hazardous chemical administered to mice, conflicts with the safety officers' risk assessment findings. Such a discrepancy indicates a programmatic issue that must be addressed through improved coordination by the safety office, the IACUC and the compliance oversight office. The *Guide* expects institutions to have written policies and procedures that address the safe use of hazardous materials based on the specific agents and assessed risk[1,2].

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Opportunity for Improvement

This scenario provides several areas for process improvement for the IACUC, researcher and Safety Officer. The use of containment (assumed, biocontainment) may be excessive burden for a commonly used hazardous chemical agent such as tamoxifen. The Principal Investigator (PI) is correct to question the IACUC on the inconsistent and perhaps overburdensome regulation set forth by this animal care and use program.

The IACUC and Safety Officer should first meet and review the use of tamoxifen, as well as other hazardous agents, at the institution. The group should review the type of housing options and determine what is most suitable for the various class of agents, as well as the equipment in use, cleaning/sanitization standard operating procedures (SOPs), and personal protective equipment (PPE) used. Containment housing, used for biological hazards, often includes autoclaving of bedding and equipment used to inactivate any viruses present, as well as increased PPE use. However, as tamoxifen is a chemical hazard, it might be a waste of money, time, and space in the containment housing facility to require investigators keep their animals under all of those conditions. In the case of this and other chemical hazards, an alternative cage labeling and/or designated rack, and appropriate bedding dumping process may be sufficient to protect staff from the hazard. As tamoxifen is a very common agent used in rodent research, it is likely that the institution can achieve both time and money savings with such a review, as well as improve investigator buy-in to appropriate practices.

It is critical that Safety Officers are aware of IACUC policies and practices related to use of hazards in animals. The Safety Officer should be made aware of cumulative number of projects across the program that include this agent that animal care staff may encounter, and special circumstances such as pregnant researchers or animal care staff must be considered. The Safety Officer should be aware of animal facilities, bedding dumping stations and practices, etc, to properly evaluate the exposure risk to animal care staff. Occupational Health Staff should also be included in the review of the exposure risk assessment.

COMPLIANCE CONSIDERATIONS

The Protocol Review coordinators offer the following compliance considerations:

1. What is a safety risk assessment?

The process of performing a risk assessment can be complex, but the primary goals are identifying and understanding the risks associated with the hazard, minimizing the risk of exposing personnel, decreasing the likelihood of accidents, minimizing the severity of the consequences of an exposure, and protecting the community and the environment from the hazard. A risk assessment is a subjective process that involves professional judgements that are typically provided by safety professional such as an Institutional Biosafety Safety Officer (BSO).

As mentioned previously, a common method for initiating a risk assessment is for the Principal Investigator (PI) to provide critical details regarding the risk and the associated activities through, for example, an IACUC and/or the Biosafety Committee submission[1]. Based on the risk assessment, the institution through the BSO should, for example, minimize the risks by:

- eliminating the risk associated with the agent by, for example, either replacing it with a non-hazardous alternative or diluting it to levels that are not considered hazardous to personnel,
- using engineering controls (e.g., safety cabinets and scavenging equipment),
- using administrative controls (e.g., creating isolated work areas, standard operating procedures, policies, and pro- cesses to communicate expectations) intended to mitigate risks,
- using personal protective equipment (PPE) such as safety glasses, respirators, gloves etc.

2. What does the discrepancy between the policy and exposure notice mean for the IACUC?

It is the authors' opinion that the scenario and the discrepancies between the policy and the exposure notice creates an opportunity for the IACUC and Safety programs to become harmonized, and that the overall institutional processes could be enhanced. The primary issue of confusion is not that GE and GW Universities' policies differ, but rather the containment requirement and the risk assessment simply do not convey a coherent and consistent message.

For this example and considering the risk assessment steps outlined above, it may have been appropriate for the individual performing the assessment to indicate that the first point above was satisfied (i.e., the hazard is being diluted to a level that does not pose a risk to personnel). Consequently, containment may not have been required since the agent would no longer be considered a human hazard. Similar practices could be employed during each hazard's consideration and subsequent assessment.

3. Should GEU revisit its policy on housing tamoxifen-treated mice in containment?

Yes; however the GEU's inconsistencies probably expand beyond the policy for tamoxifen-treated mice. GEU's Safety Officer, Director of Compliance, IACUC Chair and perhaps the Attending Veterinarian (AV) and the Institutional Biosafety Committee (IBC) Chair should coordinate a meeting to discuss and understand the assessment process and subsequent decision-making practices. Through this meeting, they should be able to identify and implement a practice that involves ensuring that an animal user completely understands the risks associated with any hazard they may be using. As a result, and should a laboratory exposure occur, the exposed individual is already aware of the potential complications associated with the exposure. Consequently, the post-exposure process does not include a risk assessment since it occurred at the time of approval, but rather documentation of exposure and subsequent required steps. The follow-up report may include, for example, the agent and a summary of the risks that were identified during the risk assessment process, how the exposure occurred, confirmation that the agent was used in accordance with the protocol and that appropriate risk mitigation practices were observed, and finally necessary follow-ups with a medical professional.

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A lack of a harmonious response to exposures causes confusion and mistrust in the actions of the Committee. Any changes or improvements to the use of chemical hazards at the institution should be conveyed to the researcher involved, and all animal users. Keeping an open line of communication, as well as incorporating a clear and helpful execution plan of any changes, is critical to IACUCs, Safety Officers, and Research Labs working together .as a team to help improve the research program.

Instead of a noncompliance, this incident should be looked at as an opportunity for improvement to the program. The IACUC should also consider updates to its onboarding and training processes for new labs to help remove confusion in policy variation. Finally, the PI should be shown the proper method to reach out to the IACUC before making any changes to required processes in the future.

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Check for updates

Revisit and Perfect the Policy

Dr. Virale's predicament presents several questions: what is GEU's actual policy on housing tamoxifen-treated mice? Is it an IACUC policy or a Safety policy? Is Dr. Virale truly out of compliance, and if so, with which office? These are unanswerable questions in this fictional scenario, but this plot nicely illustrates an actuality most institutions face at some time or another: policies aren't perfect. Any time a policy isn't working as intended – it is not providing clear guidance on what is expected or required in the conduct of university business – it should be revisited.

Somewhere along the way, something went wrong for Dr. Virale, and GEU should be invested in finding out why. These instances – though frustrating – present opportunity for programmatic growth. A thorough review of this policy is a reasonable place to start and should solicit input from stakeholders across the university, such as facility operations and animal users in addition to Safety and the IACUC. Regardless of the eventual outcome for the policy, this exercise of rigorous self-evaluation with participation by all invested departments is expected to strengthen the collective understanding of the policy and its rationale. This situation also invites evaluation of the Principal Investigator (PI) onboarding and animal import processes: how was Dr. Virale able to secure protocol approval, complete facility orientation, transfer animals into conventional housing, and initiate tamoxifen treatment without realizing containment was expected? Bolstering and streamlining these and related processes should be universally beneficial to the program.

GEU should critically evaluate its policy as part of the bigger evaluation of what went wrong with Dr. Virale's mice. Whether and how GEU's policy is ultimately changed would depend on several factors, among them risk assessment, operational and facility constraints, other university policies, and GEU's unique balance of risk aversiveness and convenience. But it should meet the goals of protecting personnel, animals, and the university by providing clear expectations. Approaching these challenges with curiosity, openness, and a collaborative spirit can foster a culture of trust, respect, and constant growth in animal programs.

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