

# The Matters of an Occupational Health and Safety Program

Dr. Mismo Virale was shocked when he was notified that an allegation of non-compliance was reported for animal activities in his lab; although Virale is a new faculty hire at Great Eastern University (GEU), he has over 20 years of experience in conducting basic science and animal research. According to the IACUC office, Virale's lab technician, Li Wang, was holding animals in standard housing instead of the required containment housing (the error was caught 24 hours after injection). Virale's animals, which were housed alone in his own vivarium housing room, were administered a low dose of tamoxifen, and never in his past 20+ years were these animals required to be housed in anything other than standard housing. A safety risk assessment was performed by the biosafety officer (BSO) and it was determined that there was no actual risk of staff exposure; the cages had not been opened or changed and

no exposure to personnel occurred in the 24 hours. Nonetheless, GEU's IACUC saw this as a serious non-compliance (improper containment of a hazard and potential risk to human safety) and decided to suspend Li Wang for one month with mandatory retraining.

Just two days later, Dr. Otra Ipotesi, another Principal Investigator (PI) in Virale's new department, hosted the IACUC semi-annual inspection of their animal use lab space and the inspectors found one lab member wasn't wearing safety glasses and the eye wash station wasn't flushed in the prior month. The inspection findings were routed to Ipotesi, via the e-IACUC system. Ipotesi responded that the eye wash had been flushed and that he spoke with his lab about the importance of safety and wearing appropriate personal protective equipment (PPE). During a departmental faculty meeting, the department chair

discussed all the animal- and IACUC-related matters with the faculty. Virale was furious when he found out that Ipotesi wasn't penalized for his safety matters while his tech was suspended.

Virale emailed the chairs of the IACUC and the Institutional Biosafety Committee (IBC) and demanded an explanation for the unfair treatment. Not that he wanted Ipotesi to get into trouble, but both labs had issues with lab safety and Virale's error didn't affect animals or their welfare. Why were two occupational health and safety matters treated so differently? □

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# Effectiveness and Consistency of Occupational Health Safety Programs

Several concerns jump out quickly, and several trigger the need for clarification which may serve to launch discussions to improve the culture of safety associated with approved animal procedures.

First, tamoxifen is classified as a hazardous drug and a known human carcinogen, teratogen, and mutagen according to the National Institute for Occupational Safety and Health. The GEU's IACUC response indicated they take mishandling of tamoxifen seriously. Personal protective equipment (PPE) recommended for handling tamoxifen and injected animals include non-permeable gloves, often double, and long sleeve coats, safety glasses, and respiratory protection depending on the presence of aerosol production. GEU further required containment housing following administration.

Second, was Dr. Virale offered an onboarding session to review his animal protocols and ensure he was aware of GEU's safety guidelines? This may have alerted him that procedures for handling tamoxifen injections differ from his former institution. Lack of onboarding does not mean Dr. Virale was not at fault since he is responsible for becoming acquainted with his new institution's guidelines. Assuming GEU's guidelines are consistent with his prior institution was a mistake.

Third, was this the first allegation of non-compliance levied against Dr. Virale and Li Wang? The 1-month suspension appears excessive given the low risk of exposure to tamoxifen and for typical escalation policies, which often involve correcting and learning from errors and establishing lab protocols to prevent future occurrences.

Fourth, it would appear that the GEU IACUC arrived at different outcomes regarding personal safety concerns for Dr. Virale and Dr. Ipotesi. The IACUC ruled strongly for noncompliance involving a specific hazard with known risks but were lenient for noncompliance involving nonspecific hazards with nonuse of safety glasses and undocumented eye-wash station flushing. The GEU IACUC may want to calibrate their responses to noncompliance involving personal health and safety guidelines. From the perspective of lab personnel, frustration may arise with non-uniform oversight and adherence to safety policies, creating uncertainty regarding best practices. By absolving Dr. Ipotesi of an undocumented eye wash station flush and lack of safety glasses, is the institution saying that eye safety is less important than potential chemical exposure? Would the

A WORD FROM OLAW AND USDA

**Response from OLAW**

In this scenario, two incidents of personnel safety findings involving research with animals were handled by the IACUC with varying outcomes. In the first incident, because the IACUC-approved protocol required containment housing and the required housing was not used, it would be a reportable noncompliance to OLAW<sup>1</sup>. Such a housing change potentially impacts personnel safety and is a significant change that requires IACUC approval via designated member or full committee review<sup>2</sup>. For this specific example, the findings involving lack of protective eyewear and eyewash flushing are outside the scope of the IACUC's animal welfare focus and require corrective action but are not reportable to OLAW.

While the IACUC may, during its semiannual facility inspections or post-approval monitoring, identify safety and other regulatory concerns, further investigation, and corrective actions, including training, are the concern of oversight components responsible for enforcement of the specific safety or regulatory issues (hazardous agents, radiation, controlled drugs, chemicals, recombinant DNA, etc.). The IACUC has the discretion to recommend a corrective action in such cases but would reduce its workload by leaving the oversight to others. As mentioned by other reviewers, the PHS Policy section IV.A.1.f. and the *Guide* consider occupational health and safety critical in the oversight of research animal care and use<sup>3,4</sup>. The *Guide* expects safety equipment to be maintained properly and personnel to be trained and to use the safety equipment provided<sup>4</sup>. An effective safety program requires evaluation of the institution's research program components and the associated risks combined with coordination by the researchers, animal facility, IACUC and the safety unit(s)<sup>4,5</sup>. In this case, the IACUC should reconsider its own role in oversight and work more effectively to ensure training for new employees and enhanced cooperation with its oversight counterparts.

**Response from USDA**

This scenario presents two examples of deviations from institutional policies

regarding personnel safety in a research facility. The Animal Welfare Act does not address issues related to human health and safety. In that light, the concerns identified in Dr. Ipotesi's lab would not be cited as non-compliances or violations of the AWA regulations. While the improper housing of the treated subjects in Dr. Virale's lab does not, in itself, represent a threat to the health or safety of the animals (and therefore would not merit categorization as a "significant deficiency"<sup>6</sup>), it is nonetheless a deviation from an IACUC-approved protocol, and would be cited as such during inspection and review of the IACUC's semi-annual reports<sup>7</sup>. As both respondents noted, the IACUC and the institution would be well-served to review their policies and practices regarding onboarding and educating new faculty, and offering opportunities to ensure they are familiar with institutional guidelines and federal regulations, including the importance of thoroughly reviewing and adhering to IACUC-approved protocols. □

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7. Animal Welfare Regulations 9 CFR § 2.31(d)(8).

IACUC decide the same if Li Wang handled the tamoxifen-injected mice without safety glasses? The GEU IACUC should consider the impact of their decisions on the broader community and how non-uniform policy adherence may weaken the research safety culture.

The overall management of the animal care and use program should be the responsibility of the IACUC. Fulfillment of occupational health and safety administrative requirements falls under an institution's environmental health and safety office. The responsibility for operating research facilities and handling animals in a safe manner is the responsibility of every individual in the program. The situation described above could trigger the institution to conduct a gap assessment, to identify strengths and weaknesses of the effectiveness of the Occupational Health Safety Program (OHSP), to ensure uniform oversight, and to clarify the roles, responsibilities, and coordination of the groups named within the governance structure. The GEU IACUC should take a strong leadership role in overseeing occupational health safety, refresh priorities regarding the effectiveness and ensure consistency of their OHSP<sup>1</sup>. □

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## COMPLIANCE CONSIDERATIONS

The Protocol Review coordinators offer the following compliance considerations:

### 1. Is the IACUC responsible for these OHSP matters?

The *Guide* requires: “Each institution must establish and maintain an occupational health and safety program (OHSP) as an essential part of the overall program of animal care and use.”<sup>1</sup> In an animal care and use program (ACUP), components of OHSPs include:

- Control and prevention strategies
- Hazard identification and risk assessment
- Facilities, equipment, and monitoring
- Personnel training
- Personal hygiene
- Animal experimentation involving hazards
- Personal protection; and
- Medical evaluation and preventive medicine for personnel

Ensuring the appropriate facilities and equipment are employed and the proper PPE is utilized, are critical to protecting “the animal care and investigative staff, other occupants of the facility, the public, animals, and the environment from exposure to hazardous biologic, chemical, and physical agents used in animal experimentation.”<sup>1</sup>

Although the IACUC is not solely responsible for establishing and overseeing a program of occupational health and safety, the collaboration of the IACUC with many other institutional units (e.g., vivarium, environmental health and safety (EHS), institutional biosafety, occupational health, human resources) is essential to a successful OHSP<sup>2</sup>.

### 2. Why are housing level and proper PPE important to the IACUC?

“An effective OHSP ensures that the risks associated with the experimental use of

animals are identified and reduced to minimal and acceptable levels.”<sup>1</sup>

The IACUC is charged with ensuring that:

- All personnel involved in animal care and use “have the necessary knowledge and expertise for the specific animal procedures proposed and the species used”<sup>1</sup>, including the necessary training and skills for the use of hazardous agents;
- Written policies and procedures governing experimentation with hazardous biologic, chemical, and physical agents are in place;
- Facilities are adequate for the safe conduct of the research; and
- Appropriate PPE is provided (and utilized).

Containment levels for in vivo research with small animals must be determined through a risk assessment that is conducted by the Institutional Biosafety Committee (IBC) or staff in an EHS office, depending on the agent in use. The appropriate PPE and assigned containment or animal biosafety level (ABSL)<sup>3</sup> function to protect people, animals, and the environment from the hazards used in animal activities.

### 3. Are these matters IACUC non-compliance (even if found during IACUC semi-annual inspections)?

Regardless of which compliance or safety office is responsible for developing the policies, a successful OHSP will empower all units to help monitor adherence to safety requirements, such as Virale’s lab housing animals in the appropriate containment level and Ipotesi’s lab wearing safety goggles.

The programmatic decision of which compliance or safety office oversees the review and evaluation of an allegation of non-compliance is institutionally specific. Whether the IACUC, the IBC, or

EHS enforce compliance depends on the structure of the program. Ultimately, the institution needs to ensure that the safety measures are adhered to and that animal care and use personnel have the training and resources necessary to safely work with all materials and agents (hazardous or non-hazardous).

### 4. What could the IACUC do?

By federal directive, IACUC functions include<sup>4</sup>:

- Reviewing concerns involving the care and use of animals at the institution;
- Reviewing the institution’s program for humane care and use of animals, using the *Guide* as a basis for evaluation; and
- Inspecting all of the institution’s animal facilities (including satellite facilities) using the *Guide* as a basis for evaluation.

While these functions are required of the IACUC, as is reporting non-compliance in accordance with federal requirements, institutions can develop their own processes for remediation when cases of non-compliance occur. □

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## A Sledgehammer To Crack a Nut?

While the two issues are thematically linked to personnel safety and that they were near misses, there is also a clear distinction. Dr. Virale’s issue involved active animal use on a study while Dr. Ipotesi’s did not. In the first case, Dr. Virale’s technician, Li Wang housed animals treated with a hazard in

an area not meant to house them. Failure to comply with the requisite containment could constitute a protocol deviation<sup>1,2</sup> and may have resulted in the group incurring the IACUC’s ire. Although the impact from this non-compliance was very low, a root-cause analysis of the issue is necessary to uncover potential programmatic issues.

Several questions come to mind: how were the containment requirements communicated to the PI and team? Were the PI and his team trained in those containment requirements? If Li Wang was trained in the correct procedures at the new institution but failed to follow them, it can be addressed with retraining and possible

meaningful sanctions. However, if gaps were identified in the established processes that may have resulted in the non-compliance, that could constitute a programmatic weakness and must be corrected promptly.

I agree with the corrective plan which involved retraining Li Wang but find the month-long suspension excessive and unproductive and liken it to using a sledgehammer to crack a nut. This mandate of the IACUC could not only cause serious harm/delay to the research that was being conducted but could also result in animals potentially going to waste, which is inconsistent with the 3Rs<sup>3</sup>. The IACUC's decision in the Virale issue accomplished the desired outcome (retraining) but

the suspension did not accomplish any meaningful outcome.

The Virale issue illustrates that acceptable practices in how hazards are handled may vary amongst institutions depending upon the resources that are available. When new faculty is on-boarded, efforts to align them with the expectations at the new institution are helpful towards preventing recurrence of such issues. Finally, everyone in the Virale group should be reminded to review their protocol before they conduct any additional studies to ensure protocol adherence.

The IACUC's handling in Ipotesi's case was appropriate and pragmatic in my opinion. The PI reinforced the use of PPE and the eye wash station was

flushed, bringing both personnel and equipment up to code, which was the desired outcome. □

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