

different strains of virus. Those symptoms may include weight loss, severe nasal congestion, bacterial infection, dehydration, malnutrition and loose stool.

Many IACUC committees have agreed that a 15% weight loss is the maximum acceptable limit for many species and strains of animals. Weight loss can have a more severe affect on female ferrets than males because they are smaller (adult females weigh only ~1–2 lb, whereas adult males weigh 8–10 lb).

There are non-medical treatments that could help the animals with influenza. For example, if Gomez feels that medicinal treatment for nasal congestion will adversely affect the study, I would suggest administering saline drops into the nasal cavity of the ferrets every couple of hours. This will help the animal to breathe, allowing it to consume food and water, reducing the likelihood of malnourishment. In addition, high-calorie supplements such as Nutrical can be given. Bacterial infections should be treated by veterinary staff. Ferrets suffering from loose stool can become dehydrated more quickly. Administering a small amount (about 1–2 ml per lb once or twice per day) of plain or vanilla-flavored store-bought yogurt will help the stool return to a more normal consistency. If Gomez is still worried that these treatments may affect the experiment, he can administer saline drops, Nutrical and yogurt to a small group of ferrets before beginning the study to assess their effects.

These simple treatments can help the animals to maintain their weight and nutrition, giving them a better opportunity to recover from the virus and reducing death from adverse secondary symptoms of the virus.

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## RESPONSE

### Why use ferrets?

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This scenario poses several troubling issues. The inadequately justified use of death as an endpoint, the potential withholding of treatment for ill animals and the lack of explanation for using ferrets to test a swine vaccine must be addressed. Our responses to this scenario reflect our disagreement with Gomez' justifications for his current protocol and with the IACUC's decisions.

Based on the information provided, Gomez does not adequately justify the scientific need for death as an endpoint. Furthermore, he doesn't justify withholding treatment, because he provides no reference to confirm that treatment will confound the immune response. We note that a secondary bacterial pneumonia would likely affect the immune response more than the use of antibiotics would.

We also disagree with the IACUC's decision to allow death as an endpoint, as Gomez has provided no justification. Several questions must be answered before the use of death as an endpoint should be approved. Is the intended purpose of the vaccine to prevent illness or death? If it is to prevent illness, allowing illness to progress to death provides no additional data. What useful information might be gained by allowing the deaths of the nonimmunized controls? It is not clear that learning whether animals may spontaneously recover helps to establish efficacy of a vaccine. Presumably, the disease course of H2N3 in this species has been well-documented. Furthermore, using death as an endpoint will result in autolyzed carcasses from which little data can be acquired.

The IACUC proposed treating ill ferrets to refine the study. We note, however, that the use of antibiotics to treat secondary pneumonias may, ironically, lengthen the ferrets' distress time more than the use of humane endpoints. In addition, if the ferrets are being used to correlate outcomes of vaccine use in swine, bacterial co-infections are a common complication of swine respiratory virus infections and should be considered a variation from the model. If the IACUC insists on treating bacterial co-infections, this should be addressed experimentally as well. The IACUC should require clearly defined humane endpoints rather than relying exclusively on treatment to reduce distress. The apparent absence of specific contributions from the attending veterinarian regarding these issues is further cause for concern.

Questions concerning whether ferrets are an appropriate species for testing a swine vaccine remain unanswered. Although ferrets are currently established as the gold standard surrogate species for the study of human influenza vaccines and transmission, there is no similar relationship established with swine influenza. There may be a cost benefit associated with the use of ferrets, but if the goal of the vaccine is to reduce morbidity and transmission in swine, then the vaccine should be tested in swine. Additional questions include the following: What questions will be answered by using ferrets? Why not use the target species exclusively? Will the vaccine also be used in ferrets? In this scenario, the IACUC needs to insist that Gomez justify not only how he plans to use ferrets, but also why he is using ferrets at all.

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