

# Acute Dermal Irritation Response in White Sinclair and Hanford Miniature Swine

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## ABSTRACT

Acute dermal irritation was induced and characterized in white Sinclair and Hanford miniature swine (N = 2 per breed per study, 3 to 4 months old, all females) using a variety of known human irritants at increasing concentrations, as two pilot studies (single dose and seven-day repeat dose) to inform a larger validation study. During acclimation, the areas of the dorsum of the miniature swine to be tested were shaved, washed, and the topical dermal challenge sites were marked. Animals were administered 0.5 mL of test compound on gauze to a 4 cm<sup>2</sup> area for four hours. Following dose administration, the gauze was removed (time 0) and animals were scored using a modified Draize scoring system for erythema (0 to 4) and edema (0 to 4), with a maximum score of 8. Scoring was conducted at 1, 24, 48, and 72 hours after test article removal following the single dose and at one hour post-dose daily in the repeat-dose study. Materials tested were as follows: sodium hydroxide, formaldehyde, benzalkonium chloride, and sodium dodecyl sulfate.

## Results

In the single-dose study, all concentrations of formaldehyde and sodium dodecyl sulfate failed to show irritation in both miniature swine lineages. All concentrations of sodium hydroxide failed to show irritation in the Hanford miniature swine, while 4% sodium hydroxide caused erythema (scores of 1 or 2) starting at 24 hours in both Sinclair miniature swine. Benzalkonium chloride at 15% and 30% resulted in higher erythema and edema scores in Sinclair miniature swine when compared to Hanford miniature swine. However, benzalkonium chloride at 45% showed no difference between the lineages. No histopathological differences were observed with any treatment between the breeds. In the repeat-dose study, both Sinclair miniature swine had erythema on Day 1 (scores of 1 or 3) and edema on Day 2 (scores of 1) with 2% sodium hydroxide, while both Hanford miniature swine had a similar but blunted response delayed 24 hours. As in the single-dose study, benzalkonium chloride resulted in higher erythema and edema scores in Sinclair miniature swine.

## Conclusion

When exposed to either sodium hydroxide or benzalkonium chloride, two known human irritants, white Sinclair miniature swine display more irritation (based on erythema and/or edema scores) when compared to Hanford miniature swine. The other two known irritants had no effect under the conditions of this study. At a certain irritation threshold (e.g., 45% benzalkonium chloride), there was no difference between the lineages. Although more testing needs to be performed to confirm the results, these early tests suggest the white Sinclair miniature swine may be more sensitive to potential irritation than the Hanford; therefore, a better animal model for human responses to chemicals.

## INTRODUCTION

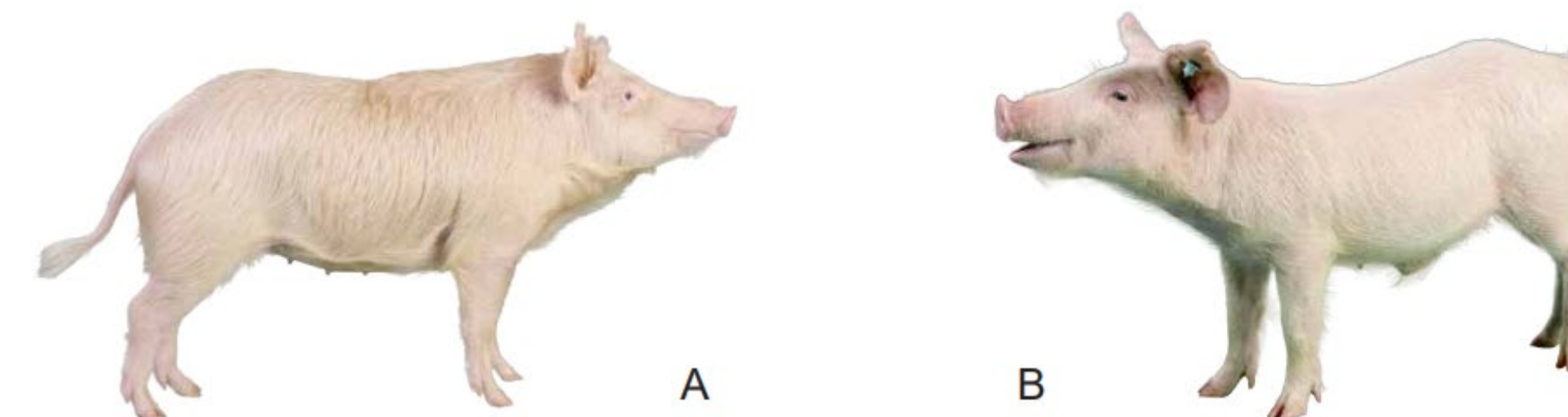
Dermal irritation is predominantly characterized by changes in erythema (redness) and edema (swelling). Chemical induction of irritation responses are concentration- and species-dependent. Traditionally, rabbits are used to evaluate new entities for the potential to induce skin irritation, as they are more sensitive than humans. Miniature swine, however, have skin that is very similar in structure and thickness to that of humans and are the non-rodent model of choice for dermal toxicology. The Hanford miniature swine is a common dermal model for regulatory submissions, due to its pink skin that is easy to score for erythema. Sinclair Bio Resources has developed an all-white variant of the Sinclair miniature swine, which could be an alternative to the Hanford miniature swine for dermal studies. The purpose of this study was to determine if known human skin irritants would induce an irritation response, and whether there was a difference in irritation response between the white Sinclair and Hanford lineages of miniature swine.

## STUDY OBJECTIVES

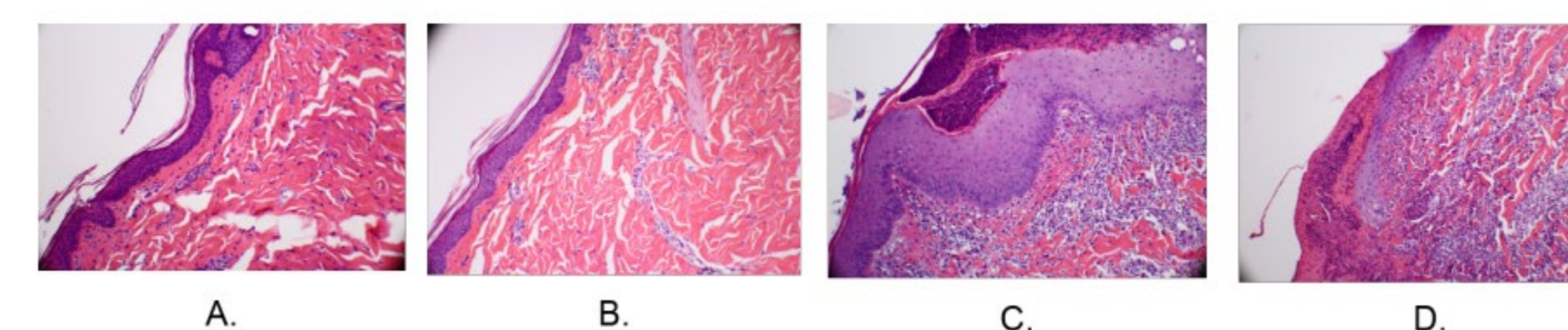
- To induce and characterize dermal irritation in white Sinclair and Hanford miniature swine with known human skin irritants
- To assess potential differences in onset or severity of irritation between the breeds

## MATERIALS AND METHODS

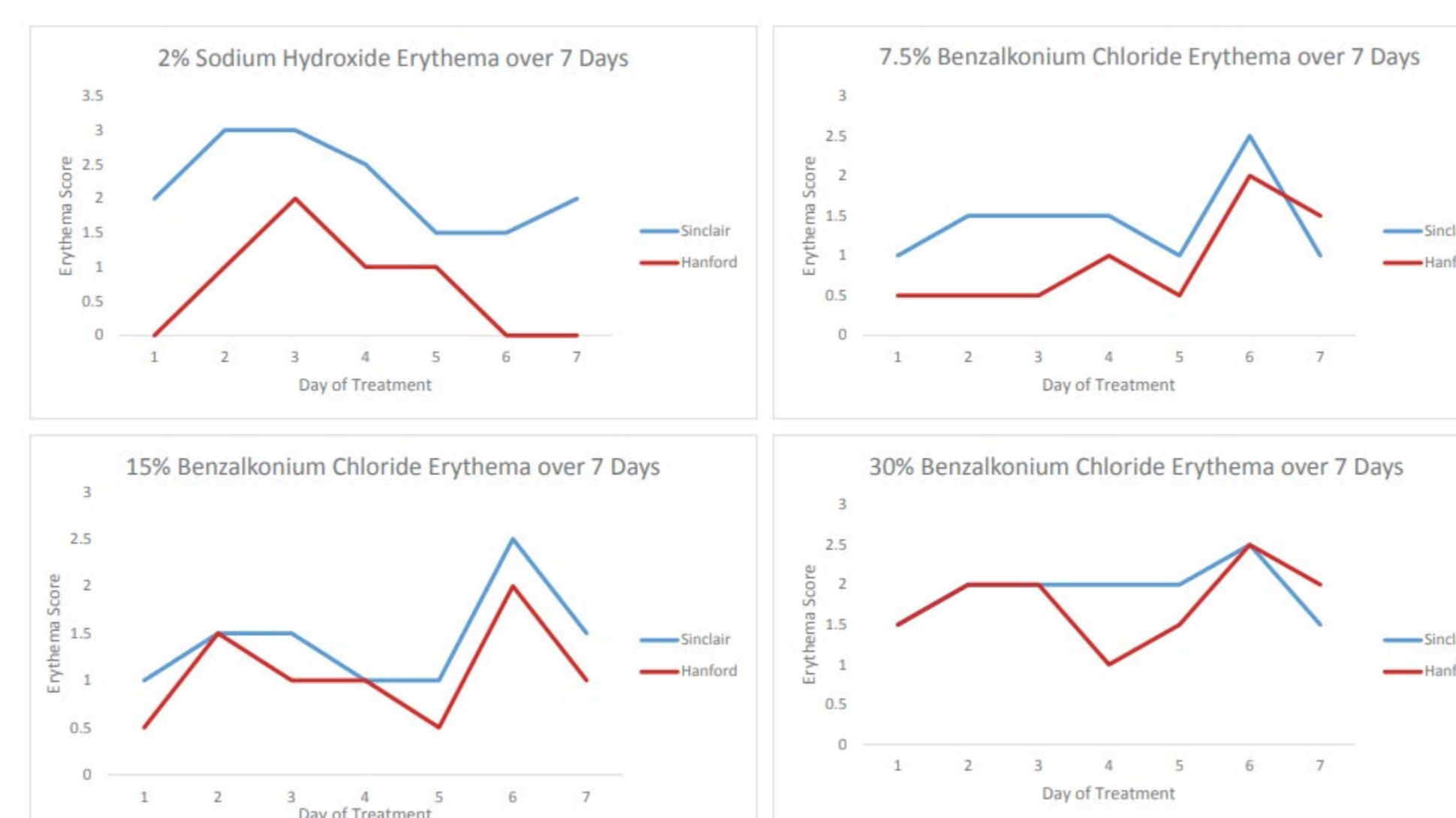
- A total of eight females (four white Sinclair and four Hanford) were used for this study. All animals were acclimated for seven days prior to the initiation of the study.
- In the acclimation period, animals were shaved, washed, and topical dermal challenge sites were marked on the dorsum.
- Treatments (0.5 mL) were applied to gauze (2 cm x 2 cm) and affixed with nonirritating medical tape. Animals were wrapped with vet wrap to keep the gauze in place.
- All treatments were removed approximately four hours after application. Treatment areas were scored with the modified Draize score for erythema and edema.
- Animals were either treated once (n = 2/breed) and scored out to 72 hours, or were treated daily for seven days (n = 2/breed) and scored daily one hour post treatment removal.
- Histopathology samples were evaluated from each treatment.



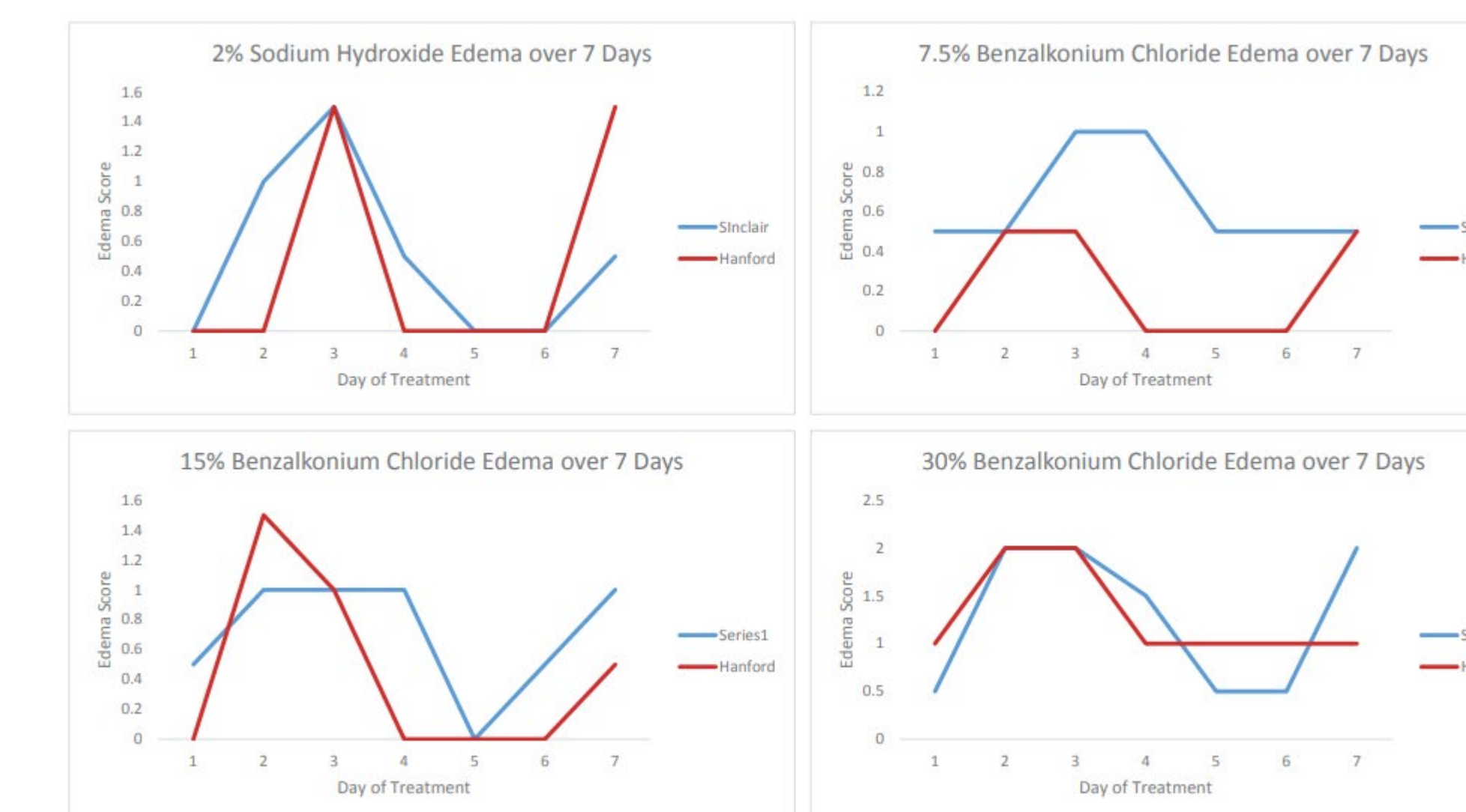
**Figure 1.** Representative images of the all-white Sinclair miniature swine (A), and the Hanford miniature swine (B). The images are not to scale and do not represent the age and/or sex of the animals used in these studies.



**Figure 2.** H&E images of white Sinclair and Hanford miniature swine skin. Sinclair normal skin (A) and Hanford normal skin (B) are similar. After a single treatment of 45% benzalkonium chloride, inflammation can be seen in both Sinclair skin (C) and Hanford skin (D).



**Figure 3.** Mean erythema scores from white Sinclair and Hanford miniature swine (N = 2 per average) for seven days of treatment with sodium hydroxide (2%) or benzalkonium chloride (7.5%, 15%, and 30%).



**Figure 4.** Mean edema scores from white Sinclair and Hanford miniature swine (N = 2 per average) for seven days of treatment with sodium hydroxide (2%) or benzalkonium chloride (7.5%, 15%, and 30%).

## RESULTS

In the single-dose study, all concentrations of formaldehyde and sodium dodecyl sulfate failed to show irritation in both miniature swine lineages. All concentrations of sodium hydroxide failed to show irritation in the Hanford miniature swine, while 4% sodium hydroxide caused erythema (scores of 1 or 2) starting at 24 hours in both Sinclair miniature swine. Benzalkonium chloride at 15% and 30% resulted in higher erythema and edema scores in Sinclair miniature swine when compared to Hanford miniature swine. However, benzalkonium chloride at 45% showed no difference between the lineages. No histopathological differences were observed with any treatment between the breeds. In the repeat-dose study, both Sinclair miniature swine had erythema on Day 1 (scores of 1 or 3) and edema on Day 2 (scores of 1) with 2% sodium hydroxide, while both Hanford miniature swine had a similar but blunted response delayed 24 hours. As in the single-dose study, benzalkonium chloride resulted in higher erythema and edema scores in Sinclair miniature swine. However, with repeated administration and increasing dose levels, the differences between the two lineages was much less pronounced.

## CONCLUSIONS

When exposed to either sodium hydroxide or benzalkonium chloride, two known human irritants, white Sinclair miniature swine display more irritation (based on erythema and/or edema scores) when compared to Hanford miniature swine. The other two known irritants had no effect under the conditions of this study. At a certain irritation threshold (e.g., 45% benzalkonium chloride), there was no difference between the lineages. Although more testing needs to be performed to confirm the results, these early tests suggest the white Sinclair miniature swine may be more sensitive to potential irritation than the Hanford; therefore, a better animal model for human responses to chemicals.

## CONFLICT OF INTEREST

All authors declare that they are employees (or were at the time of the conducted study) of either Altasciences or Sinclair Bio Resources, LLC as denoted on the poster.