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NOTICE TO USERS OF JAX® MICE

14 AUGUST 1997

C57BL/6J SKIN LESION PROBLEM ELIMINATED

Dear Colleague:

We are very pleased to inform you that in combination with previous actions, the dietary change made 14 April 1997 has resulted in a dramatic and sustained reduction in incidence of the skin lesions in C57BL/6J and related strains of mice. The overall incidence in six to ten-week-old female mice has been well below 1% for the last ten weeks. It is especially encouraging that the incidence in the nine and ten-week-old mice has been zero for the past six weeks. Not only have the inflammatory lesions virtually disappeared, but the more common predisposing alopecia has almost disappeared as well.

The skin lesions were associated with increased aggressive behavior and dominance barbering in group housed females. Groups as small as two exhibited the condition. The site of the lesions was similar for mice in the same cage, but varied markedly from one cage to the next, strongly suggesting a learned behavioral factor. The onset of the condition typically began at six weeks of age and continued for several weeks resulting in considerable hair loss through dominance barbering and, subsequently, excoriation of the skin.

The condition first appeared in May 1995; although there was a prior occurrence twenty years earlier which remitted spontaneously after several months. As soon as the condition appeared in May

1995, we undertook an intensive effort to determine and eliminate the cause. A Task Force comprising people in key research disciplines (veterinary medicine, immunology, genetics, physiology, nutrition, animal technology and engineering) as well as senior management was established and led by the Director of The Jackson Laboratory.

Several lines of investigation were followed simultaneously. A major line of investigation was directed toward the detection of infection or mutation, since either could have serious consequences for our users. Early on, we determined that there were no infectious agents, no immunologically mediated reactions and no related mutations or genetic contamination.

Because of differences in incidence between breeding rooms, environmental influences were thoroughly examined including the effects of noise, vibration, temperature, humidity, lighting, airborne contaminants, filters, water, cages and water bottles. No departures from normal environmental or operating conditions were detected and there was no correlation between these parameters and incidence of the condition in different parts of the colony.


A multi-factorial experiment was then performed which altered many standing operating conditions at the same time. The major categories of factors altered included housing, husbandry and nutrition. For example, housing changes compared pressurized individually ventilated cages with conventionally ventilated cages which resulted in changes to ventilation rate, humidity, and noise; also altered were water bottles, cage covers, cage filters and bedding; the primary change in husbandry compared weaning age at three weeks and at four weeks; nutritional effects were

compared between two diets. The experiment was conducted in a production room with the control group housed in the same room, using our standard operating conditions. (We can reassure you that no mice from the experimental group were distributed outside The Jackson Laboratory).

The results of the multi-factorial experiment when combined with results from other ongoing experiments indicated that weaning age had a significant effect. Accordingly, the weaning age of C57 lines was changed to from three weeks to four weeks in May of 1996. The incident of skin lesions dropped following the change, but not to background levels, suggesting additional factors were involved.

Concurrent with the multi-factorial experiment, we carried out a series of experiments with several diets. The early experiments clearly indicated that diet had a major influence on the skin lesions; and this was confirmed in subsequent more detailed experiments. On the merits of the experimental results, the diet was changed April 14, 1997 to N.t.H.#31, 6% fat. Within three weeks the incidence of lesions dropped to less than half the previous rate, which had been about 5.5%. The incidence continued dropping rapidly, and for the past several weeks has been well below 1 percent through 10 weeks of age. The appearance of the mice has vastly improved, with sleek thick coats once again the norm.

The mice will, of course, continue to exhibit juvenile alopecia and, in older mice, barbering; both of which are normal strain characteristics of C57BL/6J and C57BL/10J lines. When excoriative dermatitis is seen, it continues to affect several mice within a cage typically at the same site. We believe this is learned behavior transmitted to the group members. We suspect that additional



environmental factors, in addition to the three already identified (weaning age, diet and learned behavior), may influence the very low background incidence we now see. Our investigation continues in an effort to identify these factors, and we plan to prepare a detailed description of our findings upon the conclusion of our studies.

As we have reported to you in earlier updates on this problem, we are very sorry for the difficulties this condition has caused in the past. We are very pleased and relieved that this condition has been reduced to background levels and we look forward to serving your research needs.

Sincerely,

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