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April 11, 2005

Dear Sir or Madam:

I am updating you with additional information regarding intestinal lesions identified in retired breeders of the C3H/HeJCr strain reported to you in the letter of March 24, 2005. We submitted 25 mice of this strain (5 – 7 weeks old) for histopathological evaluations of the intestine. In addition, we submitted 55 animals from the colony for evaluation of Helicobacter by culture and PCR. The microscopic diagnoses provided by Meredith Simons, MS, DVM, DACVP are:

<u>Mouse</u>	<u>Observation</u>
#1	<u>Ileum, cecum, colon</u> : Within normal limits
#2	<u>Ileum, cecum, colon</u> : Within normal limits
#3	<u>Cecum</u> : Typhlitis, subacute, lymphohistiocytic, multifocal, minimal <u>Ileum, colon</u> : Within normal limits
#4	<u>Ileum, cecum, colon</u> : Within normal limits
#5	<u>Ileum, cecum, colon</u> : Within normal limits
#6	<u>Ileum, cecum, colon</u> : Within normal limits
#7	<u>Ileum, cecum, colon</u> : Within normal limits
#8	<u>Ileum, cecum, colon</u> : Within normal limits
#9	<u>Ileum, cecum, colon</u> : Within normal limits
#10	<u>Ileum, cecum, colon</u> : Within normal limits
#11	<u>Ileum, cecum, colon</u> : Within normal limits
#12	<u>Ileum, cecum, colon</u> : Within normal limits
#13	<u>Ileum, cecum, colon</u> : Within normal limits
#14	<u>Ileum, cecum, colon</u> : Within normal limits
#15	<u>Ileum, cecum, colon</u> : Within normal limits
#16	<u>Ileum, cecum, colon</u> : Within normal limits
#17	<u>Ileum, cecum, colon</u> : Within normal limits
#18	<u>Cecum</u> : Typhlitis, subacute, neutrophilic, multifocal, mild <u>Ileum, colon</u> : Within normal limits
#19	<u>Ileum, cecum, colon</u> : Within normal limits
#20	<u>Cecum</u> : Crypt abscess, focal, minimal <u>Ileum, colon</u> : Within normal limits
#21	<u>Ileum, cecum, colon</u> : Within normal limits
#22	<u>Ileum, cecum, colon</u> : Within normal limits
#23	<u>Cecum</u> : Typhlitis, subacute, neutrophilic, multifocal, minimal <u>Ileum, colon</u> : Within normal limits
#24	<u>Ileum, cecum, colon</u> : Within normal limits
#25	<u>Ileum, cecum, colon</u> : Within normal limits

Dr. Simons interpretes these findings as follows:

“There are no lesions of significance in these tissues, nothing resembling the inflammation and dysplasia in the large intestine of C3H/HeJCr retired breeders in the barrier. The few minor lesions in these younger mice are considered to be incidental findings.”

The Helicobacter testing, conducted in the Animal Health Diagnostic Laboratory of NCI-Frederick found that 55 of 55 C3H/HeJCr did not have detectable organisms by culture or by PCR testing.

These data indicate the 5 – 7 week old C3H/HeJCr mouse does not have the gastrointestinal lesions recently reported in the C3H/HeJCr retired breeders. We have also concluded that the lesions in the retired breeders are not due to infection with Helicobacter. Whether these lesions are the result of a genetic predisposition in this breed for gastrointestinal lesions cannot be confirmed; however, we continue to consider these lesions to be consistent with those reported by Sundberg et al. (Gastroenterology 1994; 107:1726-1735). Further studies will determine whether occult blood tests will identify breeding animals with lesions.

In light of these findings, we believe providing 4 – 8 week old C3H/HeJCr to the research community provides no identifiable health risk to rodent colonies. We urge each user to assess whether the findings reported here may impact their research objectives.

As additional information becomes available we will continue to inform the research community using these mice. If you have questions or concerns please contact Linda Blumenauer at (301) 846-1153.

Sincerely,



Melinda G. Hollingshead, D.V.M., Ph.D.  
Chief, Biological Testing Branch

enc: letter of March 24, 2005

cc: L. Blumenauer  
B. Curry  
J. Herring  
M. Ahalt