Mallard House, Kings Pool, 3 Peasholme Green, York YO1 7PX,
Website: www.pesticides.gov.uk
Switchboard: 01904 640500 GTN: 5138 5886
Direct Dial: 01904 455886 Fax: 01904 455711
International: (+44) 1904 455886 International Fax: (+44) 1904 455711
Email: t.j.holmes@psd.maff.gsi.gov.uk

To: All MAFF Approval Holders

cc: Interested Parties for Information

Our Ref: AAHL/32/2000

Date: 12 October 2000

Dear Sir/Madam

LONGEVITY OF RATS IN CARCINOGENICITY BIOASSAYS

In March 2000 the Department of Health Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment (CoC), considered the longevity of rats in carcinogenicity studies and were aided in doing-so by a database prepared by PSD.

The proper conduct of carcinogenicity studies in rats is an important part in the evaluation and prediction of potential human carcinogens. For a negative result from a rat carcinogenicity bioassay to be considered acceptable in accordance with EU and international guidelines, survival at 24 months should be 50% or greater in all groups. Significant reductions in the number of rats (including controls) surviving to termination have been widely reported in the scientific literature. This is a matter of concern since the power of a study to detect effects reduces as the number of animals decrease. Inadequate carcinogenicity studies could be important in any decisions regarding the identification of potential human carcinogens and in particular the failure to identify such compounds. In addition there is a possibility that inadequate studies could be rejected by regulatory agencies with the consequent need for use of further animals to obtain a more statistically valid result.

PSD reviewed survival in control animals from 26 carcinogenicity studies in rats which had been submitted over a period of 1993-1998. These carcinogenicity tests had been undertaken between 1983 and 1995. Of these studies 18 had used Sprague-Dawley rats (from various sources), six Wistar rats and two Fischer 344 rats. Adequate survival was reported for 3/18 studies in Sprague-Dawley rats, all of the studies in Wistar rats, and one study undertaken in Fischer 344 rats. Most inadequate studies had been undertaken using Charles-River Sprague-Dawley rats.

One of the conclusions the CoC reached was that unacceptable survival at termination (<50%) in carcinogenicity tests is predominantly confined to Charles-River Sprague-Dawley rats. Hence if survival in long-term carcinogenicity bioassays is to be compliant with current UK and EC guidelines for the acceptability of a negative result from such studies, test laboratories may wish to consider using alternative strains to the Charles-River Sprague-Dawley.

A copy of the CoC statement on the issue can be found at www.doh.gov.uk/longevity.htm. If you have any queries concerning the contents of this letter, please do not hesitate to contact me by telephoning 01904 455886, by fax on 01904 455711, by e-mail to t.j.holmes@psd.maff.gsi.gov.uk, or in writing to the above address.

Yours faithfully

TOM HOLMES
Toxicology and Exposure Branch