E4

The 67 dogs assigned to column E of this report were included in toxicology or safety assessment procedures in which, to meet Food and Drug Administration requirements under Good Laboratory Practice regulations (21 CFR 58.120, 43 CFR 60013) a limited number of animals must be exposed to test compound dose levels toxic to the animal. Clinical signs produced by some test compounds at toxic dose levels may be distressful or painful to the animal, if only transiently. To intercede prematurely would invalidate the procedure, requiring its repetition and the consequent use of more animals.

The 491 guinea pigs assigned to column E of this report were included in toxicology or safety assessment procedures in which, to meet Food and Drug Administration requirements under Good Laboratory Practice regulations (21 CFR 58.120, 43 CFR 60013) positive control animals must be sensitized, then challenged by intradermal injection resulting in a transient inflammatory response, which may be distressful or painful to the animals albeit for a strictly limited period. To intercede prematurely would invalidate the procedure, requiring its repetition and the consequent use of more animals.