

ment. The generally accepted method for chemical carcinogenicity testing is a time-consuming (about 3 years) and costly (\$350,000+) process using 400-800 animals, usually rats and/or mice. The Environmental Protection Agency lists over 40,000 chemicals in current widespread use. This list is growing at a rate of 500-1,000 per annum. Only 3,500 chemicals have been adequately tested in animal assays, and with the presently available resources, only 500 chemicals could be assayed in this manner each year (T.H. Maugh, *Science* 201: 1200-1205, 1978)

If consumer demands are to be met, quicker assays must be designed. Hence the interest in the development of tests using cell systems. However, this interest in alternative systems could also be a boon to animal welfare. As Professor Marquardt himself has argued in discussing the need for *in vitro* assays, "Any extension of animal testing on such a wide scale [to cover all environmental chemicals] would be vigorously opposed by animal welfare lobbies. Animals will benefit from the development of such alternative ways to the use of laboratory animals in carcinogenesis studies: The use of, and the pain and suffering to, live animals will be minimized." (H. Marquardt, *Staub-Reinhalt Luft* 38:259, 1978).

The Ames test, which employs *Salmonella typhimurium* bacteria, is based on the observation that many carcinogens also cause mutations. Thus, the end point in the Ames test is the detection of an increased number of mutant bacteria colonies on the petri plate, the hypothesis being that noncarcinogens will not cause bacterial mutagenesis while carcinogens will. Other factors have been added to the test to improve its reliability. Bacterial permeability has been increased so that the chemical will actually reach the genetic material by using *Salmonella* strains with defective cell walls. Some measure can be

made of the probable metabolism *in vitro* of the test chemicals by incorporating mammalian liver extracts in the agar which is added to the petri plate. A plasmid (an extra piece of DNA) has also been incorporated into several strains which, for an as yet incompletely explained reason, increases their sensitivity to mutational events.

The Ames test has proven remarkably successful in detecting known carcinogens although false negatives (*i.e.*, known carcinogens which are not mutagens) still present a problem. When used to test chemicals whose carcinogenicity or noncarcinogenicity has already been determined by animal assays, the Ames test has a success rate of approximately 90%.

Certain mammalian cell transformation systems also have an impressive record of success. According to Professor Marquardt, the mammalian cell systems are "perhaps the most promising new systems for the bioassay of chemical carcinogens and for the analysis of their mechanisms..." While the *in vitro* transformation system is perhaps the closest that one can come to an *in vitro* induction of a carcinogenic event, it is not necessarily the case that morphological transformation of the cells is equivalent to malignant transformation (tumorigenicity) in animals. For this reason, morphologically transformed cells are periodically injected into live animals to confirm that they do indeed cause tumors. In his own work, Professor Marquardt uses a cloned line of C3H mouse fibroblasts (M2) which are susceptible to malignant transformation by chemicals, characterized by a marked change in their morphology. Professor Marquardt's research has focused on questions relating to the mechanism of carcinogenesis and the microsomal metabolism of carcinogenic chemicals. However, his results indicate that the cell test is in substantial agreement with animal tests, and he

refers to other studies in which agreement exceeded 91%.

In December, 1979, the National Institute for Environmental Health Sciences announced the results of an international evaluation of five short-term tests (among them the Ames test and a mammalian transformation test) involving 60 laboratories and 42 chemicals, including 15 carcinogens paired with chemically similar noncarcinogens. The Ames test stood up quite well, but no single assay or battery of assays was shown to be best for carcinogenicity screening. However, these interim results were encouraging support for the prediction made by Peter Hutt, former Chief Counsel for the Food and Drug Administration, that "it is likely, indeed, that in time they [*in vitro* tests] will be perfected to a point where they are able to mimic human response far more accurately than animal testing" (*Food Drug Cosmetic Law J* 33:576, 1978).

## FARM ANIMALS

### *EEC Investigates Hen Batteries*

The European Economic Community (EEC) is feeling the effects of a Frankfurt, W. Germany Superior Court decision on keeping hens in battery cages. The Court ruled in 1979 that battery caging prevents the hens from expressing normal behavior patterns and therefore may in future be punishable under a section of the German Animal Protection Law (See *Bulletin of the Institute for the Study of Animal Problems* 1[7]:4, 1979). Pressure in the Federal Republic of Germany from both the animal welfare lobby and poultry farmers currently using batteries prompted the government to request a ban of battery cages for laying hens throughout the Common Market.

The European Agricultural Ministers responded by setting up a working party to conduct a general survey

of egg production methods, to present a proposal for transitional regulations in the move toward a total ban on batteries in the EEC, and to promote sound alternative production systems. September 1981 was the original due date for the working party's report, but the deadline was moved forward to September 1980 at the urging of German Agricultural Minister Josef Ertl.

According to the British publication *Ag* (No. 56, November 1979), the National Farmers Union is concerned about this turn of events, fearing that the new deadline will force an inadequate analysis of the issue. However, the UK, along with Denmark and The Netherlands, has registered its support for speeding up the enquiry.

### *Oregon Disease—A Possible Welfare Solution*

Ischaemic necrosis of the breast muscle of adult turkeys, broilers and also spent turkey layers ("Oregon disease") results in considerable economic loss, both in North America and in the UK. Hitherto, no practical method to prevent this disease has been found. However, P.A.L. Wight, L. Martindale and W.F. Siller (*Vet Rec* 105:470-471, 1979) have presented extremely promising data which demonstrate that the incidence of Oregon disease can be significantly reduced by modifications in husbandry.

Rearing birds in a quiet environment with familiar, gentle handlers, and subjecting them to minimal disturbances resulted in an 0.68% occurrence of the disease, as compared to approximately 16.2% under commercial conditions. The authors also suggest that tranquilization prior to certain procedures might repay further investigation.