

in various test systems, but we believe that none has had the kind of systematic testing that would be regarded as adequate. Such testing, we believe, is entirely practical and feasible. There are numerous widely used test systems that are precise, efficient and relatively inexpensive. However, these mainly depend on microbial, insect, or plant systems and there is a question as to their relevance to man. For definitive testing, it is necessary to use systems that have a high degree of presumptive human relevance. We believe that such satisfactory systems now exist, that are practical, sensitive and relevant. In this report, we recommend that a combination of these be routinely applied to all pesticides.

METHODOLOGIES FOR MUTAGENICITY TESTING

A variety of methodologies are now available for mutagenicity testing. From the criterion of presumptive human relevance, they have been categorised as ancillary systems and as mammalian systems. The human relevance of data obtained from ancillary test systems is uncertain, in view of factors such as cell uptake, metabolism, detoxification, dosage, and method of administration. The mammalian systems embody fewer of these drawbacks.

Since no single method can detect all possible types of mutations, a combination of methods must be used. A positive result in *any* of the mammalian systems represents evidence of a potential mutagenic hazard. The danger inherent in the use of restricted and inappropriate test systems is apparent from recent contract-supported studies in which mutagenic activity of pesticides was tested in microbial systems. In these studies, the microbial systems could have detected only point mutations, whereas structural considerations indicated that the pesticides tested could only induce inactivating DNA alterations resulting in chromosome breaks and aberrations. Additionally, some of the pesticides required microsomal enzymatic activation which could only occur in *in vivo* mammalian test systems.

In addition to these test procedures, human population monitoring may reveal mutagenic effects of pesticides or any other environmental agents that have escaped detection.

Ancillary methods

Bacterial.—A variety of relatively simple and inexpensive tests are available for demonstrating point mutations. (1) However, these systems are generally insensitive to chemicals inducing chromosome breakage in higher cell forms. Reverse and forward mutations are generally tested using biochemical markers; additionally, drug resistance is used as a marker for forward mutations. These methods include: