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Topical Report

Evaluation of the Mouse Micronucleus Test

As Compared with the In Vivo Cytogenetics Test for
Mutagenicity of Synthetic Fuel Materials

March 9, 1980

MASTER

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PURPOSE

This brief topical report provides information on a comparison of the mouse micronucleus mutagenic test proposed by a DOE contractor (FMC) for coal derived chemicals; as compared with the in vivo cytogenetic test. The latter procedure is reportedly preferred by EPA authorities connected with implementation of the toxic substances control act (TOSCA). This evaluation was performed at the request of Headquarters DOE program management staff. The mouse micronucleus test takes less time and costs approximately one fourth that of the in vivo cytogenetic procedure. This topical report is written to the extent possible in non-technical language to present conclusions associated with the evaluation rather than a detailed scientific dissertation.

SUMMARY OF ACTION FOR THE EVALUATION

A review of the rationale for the use of the micronucleus test, proposed by the Chemical Research and Development center, FMC, and their protocols for the coal derived chemical toxicology program was reviewed by the AFMA Scientific Advisory Board. Following that, interviews and personal communications were initiated with eight recognized scientific experts in the field of mutagenic testing. Reviews were then made of the scientific proceedings of a peer review committee concerned of the scientific literature cited by FMC in its rationale. Other data, including unpublished proceedings of a peer review committee concerned with mutagenic testing, were also examined. A listing of the individuals consulted is provided in Attachment 1.

CONCLUSIONS AND RECOMMENDATIONS

The Scientific Advisory Board Review Panel considered the following questions and, based on the available data, arrived at the conclusion stated:

1. Is there a consensus of opinion in the scientific community as to the validity of the mouse micronucleus test as compared with the in vivo cytogenetic procedure?

Opinions ranged from negative to moderately enthusiastic. Recent changes in protocols for this test, however, have made the procedure much more reliable. The consensus of opinion is that there is insufficient evidence to compare the two tests on a specific chemical basis. A false negative problem (which was noted with the micronucleus test in early work) has been resolved by new protocols which require that the changes in cells be evaluated at two, three, and four

day post-exposure periods. The micronucleus test is widely used in Europe, and is gaining acceptability in the United States because of ease of use, lower costs, and the possibility of greater accuracy.

2. In view of the above should the mouse micronucleus test be used in lieu of the in vivo cytogenetic test for mutagenicity of coal derived chemicals?

Because of the recognized problems cited in the literature and stated by most of the scientists contacted, it is recommended that the mouse micronucleus test should not be used as a single test procedure by and of itself to determine mutagenicity of coal derived materials. On the other hand, if used in conjunction with other in vivo or in vitro test procedures it should be considered an acceptable process. FMC's protocols call for such other tests as part of their overall test program. The mouse micronucleus test therefore would be satisfactory as proposed by FMC.

3. Should the possibility be considered of using both procedures for coal derived chemicals for the present proposed FMC test program?

Based on available information, the review panel believes that DOE should consider having both tests performed. One of the principal problems stated by the majority of the scientific experts contacted is that there is insufficient evidence to compare the two tests, particularly with regard to their efficacy for specific chemicals. Recent changes in the protocols for the mouse nucleus test have made the procedure more reliable, and the false negative problem has been resolved. Because of the lack of specific comparison, particularly of materials similar to or related to coal derived chemicals, the panel concludes that DOE should consider having both tests performed. This would provide direct comparison of the validity of the two procedures in regard to coal derived materials. The added cost for undertaking such tests would provide a better basis in event of further discussions with the U.S. EPA are required period.

Information developed in the course of this evaluation includes that relating to the present EPA committee review of the mouse micronucleus

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test. That information indicates that the panel studying this problem is preparing an evaluation of the procedure and developing suggested protocols for its use. The final decision as to its conclusion by EPA in its approved procedures is, of course, an EPA policy decision. If as suggested above both tests are undertaken, DOE would have a better scientific basis for any further actions with EPA on this matter. Further in event the mouse micronucleus test was not approved by EPA a "fallback position" would be available which would avoid delays of possible interference with the rest of the FMC protocol. The desirability of coordination with the basic research toxicology's elements of EV should also be considered in arriving at a overall DOE policy position via vive EPA.

Attachment 1

Scientific Communications--

Re Mouse Micronucleus Test

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Dr. Sheila Galloway	Litton Bionetics, Kensington, MD
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Prof. Marvin Legator	University of Texas, Medical Branch Galveston, Texas
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Dr. Beverly White	National Institute of Arthritis and Metabolic Diseases, Bethesda, MD
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