TELEPHONE HUDSON 3-6126

Manufacturing Chemists' Association, Inc.

(FOUNDED 1872)

1825 CONNECTICUT AVENUE, N. W.
WASHINGTON, D. C. 20009

November 11, 1968

TO: Food, Drug, and Cosmetic Chemicals Committee

SUBJECT: MCA Statement to Panel on Cancer Testing, FDA Advisory Committee on Protocols for Safety Evaluation

Gentlemen:

Attached is a copy of the subject statement dated November 11, 1968 for your information, which was developed by the task group composed of Drs. Treon (chairman), Shaffer, and Zapp.

Sincerely yours,

Morgan M. Hoover

MMH:sjg

Attachment

Copy to: Dr. J. T. Treon
Dr. C. B. Shaffer
Dr. J. A. Zapp

Distribution "A"

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GEORGE H. DECKER
General U.S.A. (Ret.)
PRESIDENT

November 11, 1968

Dr. Philippe Shubik, Director
Eppley Institute for Research in Cancer
The University of Nebraska College of Medicine
42nd and Dewey Avenue
Omaha, Nebraska 68105

Dear Dr. Shubik:

In response to your letter of September 27, 1968, the Manufacturing Chemists Association wishes to submit the following statement for the consideration of the Panel on Cancer Testing of the FDA Advisory Committee on Protocols for Safety Evaluation. The Manufacturing Chemists Association is a nonprofit trade association of 181 United States and 12 Canadian company members representing more than 90 percent of the production capacity of basic industrial chemicals within these countries.

Prior to the introduction of a new chemical food additive, it is essential that it be sufficiently tested for potential toxicity, including carcinogenicity, to insure the practical absence of adverse effects in the intended use of the material. The tests should not be so insensitive as to lead to the acceptance of a dangerous substance; on the other hand, they should not be so sensitive as to lead to the rejection of a substance which does not present any significant hazard to the consumer.

Therefore, the perspective of the industrial toxicologist is different from that of the investigator engaged in research on the mechanism of cancer. We must allocate the limited funds, time and personnel to those procedures which we feel are most likely to yield meaningful results.

Carcinogenicity is only one aspect of testing for chronic toxicity. We believe that it should be conscientiously looked for in the course of all tests performed to evaluate the chronic toxicity of a substance. If a chemical, food, or cosmetic additive produces no hint or suggestion of carcinogenicity in the course of all the tests currently required for the evaluation of the safety of such chemical additives, additional specific tests by other techniques or different routes of administration appear to us to be an unnecessary burden unlikely to produce results of practical significance.

In reply to the questions in your September 27, 1968 letter, we have the following comments (numbers correspond to yours):

1. Specific pathogen free rats are desirable because they permit longer survival and less complication with incidental disease and parasites. We do not

consider germ free animals desirable because they do not provide a system that simulates a condition in man.

2. The dog should not be used for routine testing but it might be employed for confirmatory testing. Although the dog is unique in responding to bladder tumorigens, a test with the dog is unnecessary to demonstrate the carcinogenicity of compounds known to cause bladder tumors in dogs and man, since rats will respond to aromatic amines with tumors in other locations.

3. We are unaware of any animal species not now commonly used that would give any more relative information than that obtained on the rat.

4. We do not know of any standard semi-synthetic diet that could be appropriate for all studies of carcinogenicity. However, we recognize that for certain compounds particular semi-synthetic diets might be expected to give a faster and greater response than normal diets.

5. The new born animal is more susceptible than the older animal. This may lead to a false positive result in some cases and lead to the rejection of an otherwise valuable material. Because the liver microsomal enzymes and other adaptive mechanisms of the new born are insufficient, the usage of such animals should not be regarded as generally applicable but might be useful in particular instances.

6. Although we do not down-grade the importance of tissue culture which may be useful for certain biological research purposes, we believe it is too artificial for routine use as a substitute for intact animals. Tissue culture is devoid of nervous and hormonal control and lacks access to the circulatory and excretory systems that integrate the intact animal.

7. If a feasible test that would simultaneously cover studies for reproduction, teratogenicity, mutagenicity, and carcinogenicity could be devised, it would be highly desirable but we are not aware of any such test at this time.

8. There is always need for a better source of laboratory animals.

We trust that these comments will be helpful, and thank you for this opportunity to express our views.

Sincerely,

G. H. Decker