NTP Public Meeting on Hexavalent Chromium Recommendations for the Proposed Studies of Hexavalent Chromium Carcinogenicity and Toxicokinetics Developed by the Expert Scientific Panel

The National Toxicology Program (NTP) held a public meeting on July 24, 2002, at the National Institute of Environmental Health Sciences in Research Triangle Park, North Carolina. The purpose of this meeting was to gain input from a panel of scientific experts (listed below) and the public about data available from preliminary studies on hexavalent chromium (CAS number 18540-29-9) and about the design of proposed laboratory carcinogenesis and toxicokinetic studies of hexavalent chromium administered in drinking water to rodents.

The Expert Panel

Dr. Robert A. Howd	California Environmental Protection Agency
Dr. Jerrold A. Last	University of California at Davis
Dr. Ernest E. McConnell	ToxPath, Inc.
Dr. Steven R. Patierno	The George Washington School of Medicine
Dr. Katherine Squibb	University of Maryland at Baltimore
Dr. Michael P. Waalkes Panel chairperson	National Cancer Institute

The experts reconfirmed the need for the study of hexavalent chromium in drinking water noting that this study provides an opportunity for evaluating two different routes of exposure, inhalation versus drinking water, and determining whether or not carcinogenic hazard by these two routes is equivalent. Overall, the experts felt the proposed two-year rodent cancer study and the special toxicokinetic study were well designed, but provided recommendations on elements that they thought could be improved.

Recommendations

Several recommendations were developed during the presentation of remarks by the expert panel and in the general discussion afterwards. For some recommendations there was complete agreement of the panel while for others there was less than complete agreement. The recommendations are listed below.

A. Recommendations for which there was complete agreement:

1. The panel uniformly recommended that the NTP include a significantly lower lowest dose than the ones proposed (125 ppm in rats and 62.5 ppm in mice as sodium dichromate dihydrate) for the two-year carcinogenesis study. It was proposed that this could be accomplished by including several additional lower doses, or by using the same number of doses but with a wider spacing than proposed (one, one-half and one-quarter). The panel was hesitant to propose specific doses, but suggested that they be below the 62.5 ppm dose and perhaps in the range of 25 or 10 ppm (one member thought

the low dose could perhaps be set lower than 10 ppm). It was felt that the lower dose or doses would potentially establish a no observed effect level for regulatory use.

2. The panel recommended that the NTP include measurement of target tissue chromium in rats and mice in the two-year carcinogenesis and the special toxicokinetics studies.

3. The panel recommended that the NTP perform blood chemistry analysis in the two-year carcinogenesis and the special toxicokinetic studies.

4. The panel recommended that the NTP not use guinea pigs as test animals.

B. Recommendations for which there was less than complete agreement:

1. Buffer the chrome solution prior to administration.

2. Utilize one sex in the two-year study and devote the consequentially preserved resources to expanding the dosage groups in the one sex of animals used.

3. Test for *Helicobacter* in mice and rats.

4. Employ a dissecting microscope in the processing of stomach samples for histopathological analysis.

5. Increase the highest dose in the mouse (one member proposed this recommendation while several spoke against it).

6. Use a "stop" group that would not be exposed to hexavalent chromium from one year onward to look at regression of lesions of the stomach and other potential targets.