NATIONAL TOXICOLOGY PROGRAM

"HORMONALLY-INDUCED REPRODUCTIVE TUMORS: RELEVANCE OF RODENT BIOASSAYS" WORKSHOP

MAY 22-24, 2006
MARRIOTT RALEIGH CRABTREE VALLEY
4500 MARRIOTT DRIVE, RALEIGH, NORTH CAROLINA

WORKSHOP CHARGE AND BREAKOUT GROUP QUESTIONS

Workshop Charge

The workshop's overall goal is to determine the adequacy and relevance to human disease outcome of rodent models for four types of hormonally-induced reproductive tumors (ovary, mammary gland, prostate, and testis).

Breakout Group Questions

1. **Is there sufficient evidence to conclude that these tumors of the reproductive system in humans and experimental animals can result from an altered endocrine milieu (i.e., steroid and pituitary hormones)?**
    a. Are tumor characteristics and the diagnostic criteria for tumor identification the same between rodents and humans? If not, what are the differences?

2. **How useful are rodent models for predicting hormonally-induced reproductive tumors in humans?**
    a. What pathological and physiological changes observed in rodent bioassays are assumed relevant for human predictions?
    b. Are there any pre-neoplastic (e.g., hyperplasia) events observed in rodents that are considered predictive of human response?

3. **What do we know of the proposed modes of action for the induction of these tumors in rodents or humans?**
    a. Are there key events in the mode of action for hormonal tumors in general, or are they specific for each tumor type? If so, what are the common modes of action?

4. **Exposure in the standard NTP rodent cancer bioassays typically commences with young adult animals. Are there any specific modes of action, or tumor types, for which an *in utero* exposure component should be the default experimental paradigm?**
    a. How would we best design such studies? (time permitting)

5. **The default approach for most cancer risk assessments is to assume linearity at low dose-response. Is this appropriate for these modes of action and tumor types?**
    a. If not, what evidence would be required to move away from the default approach?
    b. How do we (or should we) incorporate the concept of "additivity to background" when endogenous hormones are present with homeostatic control mechanisms?