Breakout Group 2

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Objective

Solicit comment on issues related to the proper interpretation of results from "transgenic" cancer models, the implications of these findings for public health decisions, and the most appropriate interpretive language to describe the results of such studies to the scientific/regulatory communities and the public

Questions

When the NTP conducts toxicology and carcinogenesis studies in traditional rodent models, it applies specific criteria for evaluating the histopathologic endpoints for carcinogenicity (Attachment 1). The endpoints scored in cancer studies conducted in genetically modified mouse models range from benign tumors, such as skin papillomas, to clear malignancies. These models all harbor genetic alterations that cause them to express tumors more rapidly than their wild type counterparts. The NTP is concerned about the appropriate interpretive language that should be used to best describe the findings from studies in genetically altered mouse models and whether it would be different from that used for traditional rodent bioassays.

For Breakout Group 2, the NTP developed some model-specific illustrations of possible outcomes from studies conducted in genetically modified mouse models. These illustrations (#1-11) follow below, along with an example from a standard 2-year bioassay (#12). For each scenario, the NTP would like this group (1) to provide their interpretations of the findings and (2) to provide the specific interpretative language that should be used to convey the study's conclusions. In addition, the NTP asks members to consider the following two general questions as they evaluate and discuss the model-specific illustrations.

1. Does the scientific/regulatory community consider tumor findings in genetically modified mouse models as equivalent to tumor findings in traditional rodent cancer models? Is the answer the same for all commonly used models (Tg.AC, p53+/-, rasH2)?

2. To what degree is the scientific/regulatory community confident that negative results in studies with genetically modified mouse models are equivalent to negative results in the traditional bioassay?