Spongiosis Hepatis/Cystic Degeneration Preneoplastic or Non-Neoplastic Lesion

Scientific Assessment

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Biological Characteristics and Potential
Spongiosis Hepatis / Cystic Degeneration

- In 1980s, lesion was considered to be not
  - Neoplastic
  - Preneoplastic
- In 1990s, lesions previously termed spongiosis hepatis were interpreted as “spongiotic pericytoma” by one experimental group that studied the genotoxic agent N-nitrosomorpholine (NNM) (American Journal of Pathology 146:903-913, 1995)
  - ➢ However, multiple limitations of this publication as addressed in written statement

Biological Characteristics and Potential
Lack of Corroborating Data to Redefine Spongiosis Hepatis to Neoplasia or Preneoplasia

A lesion progressing from spongiosis hepatis to clear neoplasia has apparently never been noted by practicing toxicologic pathologist.

- No primary publication describing a rodent neoplasm that had histological characteristics to support origin from spongiosis hepatis
- A lesion progressing from spongiosis hepatis to clear neoplasia was not described in recent compendium of rodent liver lesions (Toxicologic Pathology 38:5S-81S, 2010)
- Tumors arising from liver pericytes (Ito cell tumors) have been recognized but are morphologically different than spongiosis hepatis

Implications of Rodent Spongiosis Hepatis Determining Human Cancer Risk

- Spongiosis hepatis has not been described in human liver
  - Reduces concern that increased incidence of spongiosis hepatis in treated compared to control rats is an indicator of human risk

- Spongiotic pericytoma in human has been described in a single published report based on recent literature search
  - Histology of this lesion is substantially different than spongiosis hepatis in rats
  - Lesion in human is therefore not a counterpart to the spongiosis hepatis lesion in rats.

Conclusion of Scientific Assessment

- Spongiosis hepatis / cystic degeneration:
  - Is a non-neoplastic lesion
  - Is NOT a preneoplastic lesion
- Spongiois hepatis in the rat is not an indication of human cancer risk