Budesonide
16,17-Butylidenebis(oxy)-11-,21-dihydroxypregna-1,4-diene-3,20-dione

Budesonide is a synthetic glucocorticoid steroid for the treatment of asthma, non-infectious rhinitis, and for treatment and prevention of nasal polyposis.

Budesonide passed the animal data screen, underwent a preliminary toxicological evaluation, and is being brought to the Carcinogen Identification Committee for consultation. This is a compilation of the relevant studies identified during the preliminary toxicological evaluation.

Epidemiological data
No cancer epidemiology studies were identified.

Animal carcinogenicity data

- Two-year drinking water studies
  - Male and female Sprague-Dawley rats: FDA (2001, pp.36-37, pp. 66-67)
    - Increases in brain gliomas and primary hepatocellular neoplasms in males and primary mammary neoplasms in females (by pairwise comparison and trend)
  - Male Sprague-Dawley rats: Ryrfeldt et al. (1992)
    - Increase in hepatocellular adenomas and carcinomas combined (by pairwise comparison)
    - No treatment related tumor findings by gross pathological examination. FDA audit of study indicated several serious regulatory deficits.

- 91-week drinking water studies
    - Increase in lung alveolar/bronchiolar carcinomas in males (by trend)
    - No treatment related tumor findings in females
    - Inadequate numbers of male and female animals at risk for late occurring tumors

Other relevant data

- Genotoxicity
    - S. typhimurium reverse mutation, D. melanogaster recessive lethal mutation, and mouse lymphoma assays (negative)
    - Chromosome aberrations in cultured human lymphocytes (negative)
- Micronuclei in mouse bone marrow (*negative*)
- Unscheduled DNA synthesis *in vitro* (*negative*)

  - Budesonide is metabolized *in vitro* by human and animal liver microsomes to 21-dehydrobudesonide, which is mutagenic in *S. typhimurium*
  - *In vitro* incubation of budesonide with rat liver and brain S9 fractions results in covalent binding to tissue macromolecules

**References**
