

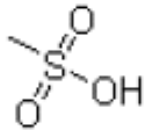
# Compounds of concern

- Alkylating agents (potential to alkylate DNA)
  - Methyl mesilate (methanesulfonic acid methyl ester)
  - Ethyl mesilate (methanesulfonic acid ethyl ester)
    - Formed by esterification of methanesulfonic acid by methanol, ethanol or other low molecular weight alcohol
    - Issue with Viracept (alcohol used in cleaning)
  - Alkyl or aryl esters of low molecular weight sulfonic acids
    - tosilates (toluene-p-sulfonic acid esters)
    - besilates (benzenesulfonic acid esters) – [PEG-esters]
    - isetionates

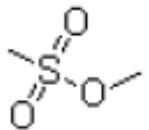
# Ethyl mesilate (Viracept - nelfinavir)

- Recall in June 2007
- MAH conducted studies in mice
- Extrapolation of data suggested threshold level of approximately 2 mg/kg/day in humans
- Patients exposed to 0.05 mg/kg/day from Viracept
- Concluded that patients were not at increased risk of developing cancer or having a baby with birth defects

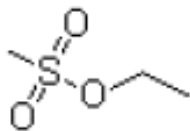
# Methanesulfonic acid Derivatives



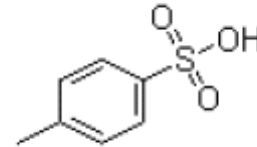
methane sulfonic acid



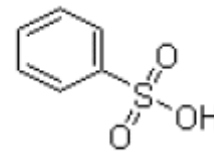
methyl mesilate  
(methyl methanesulfonate)



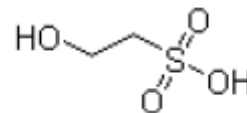
ethyl mesilate  
(ethyl methanesulfonate)



p-toluene sulfonic acid (tosic acid)  
forms p-toluene sulfonic acid esters  
(tosilates)



benzene sulfonic acid  
forms benzene sulfonic acid esters  
(besilates)



2-hydroxyethane sulfonic acid (isothionic acid)  
forms 2-hydroxyethane sulfonic acid esters  
(isethionates)