

Kidney and other Urogenital System Effects:

- 1) Sufficiency of weight-of-evidence (independent of kidney effects) for identifying the prostate as a hazard of RDX exposure:

The increase in the incidence of suppurative prostatitis and the shift from chronic prostatic inflammation to suppurative prostatitis in the Levine et al. (1983) study were dose-related and the trend statistically significant, starting at the 1.5 mg/kg-day dose; and they remained significant even if the highest dose-group was not considered because of its high mortality. No prostate effects were reported in any of the other animal studies with RDX, but the Levine et al. study was the only chronic (long-term) study with rats and severe kidney effects were also only observed in this rat study; renal effects found in other studies were far less severe. Thus, the rat was the only species selectively susceptible to severe effects of RDX on the genitourinary system. The weight-of-evidence for identifying the prostate as a hazard of RDX exposure is sufficient since the effects on the prostate were dose-related and statistically significant, albeit limited to the rat.

- 2) Prostate endpoint that would be most appropriate for analysis (suppurative or all types of prostatitis combined)

The prostatic endpoint of all inflammation combined was not changed with increasing RDX dose, except at the highest dose (40 mg/kg-day), where its incidence was increased to 21/31 (68%) from 22/54 (41%) in controls ($p = 0.024$; two-sided Fisher's exact test). Only the incidence of suppurative inflammation and the shift from chronic to suppurative prostatitis were significantly increased at lower dose levels (1.5 mg/kg-day and above). Both of the latter endpoints would be appropriate for analysis, but the suppurative prostatitis incidence data would probably be the most appropriate for quantitative risk assessment based on dose-response data.