

Public Comments on the Nomination of Vanadium Compounds

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Vanadium's oral toxicity is low

- ▶ *“There are very few reported cases of vanadium toxicity in humans where exposure has not been by inhalation.”*
 - Expert Group on Vitamins and Minerals, U.K. Food Standards Agency, 2002.
- ▶ Reversible effects with human volunteers consisted of abdominal pain, nausea, and weight loss.
- ▶ NIEHS cites human data showing absorption to be 1% or less.

Typical exposures are below levels that might reasonably cause concern

- ▶ The National Academies' Institute of Medicine (2001) established an upper level (UL) of 1.8 mg/day.
 - Based on an LOAEL of 7.7 mg/kg/day for renal toxicity in rats and an uncertainty factor of 300.
- ▶ Consistent with other studies:
 - Domingo JL, et al. (1991) showed vanadyl and metavanadate treatment (at 6.1 and 22.7 mg/kg/day, respectively) were associated with rises in serum urea and creatinine concentrations.
 - Boscolo P, et al. (1994) showed metavanadate treatment at 10 and 40 ppm were associated with a decreased Na⁺, K⁺-ATPase activity, increased urinary excretion of potassium, increased plasma renin, urinary kallikrein, kininase I, and kininase II activities, and increased plasma aldosterone.

Typical exposures are likely to be 30 – 180 fold lower than the UL or 9000 – 54,000 fold lower than the LOAEL.

Typical exposures are below levels
that might reasonably cause concern

- ▶ NIEHS cites the mean intake of vanadium through drinking water to be only 8 µg/day.
 - Even the highest value cited – 140 µg/day – is still more than 10-fold lower than the UL.
- ▶ Weight training athletes may use up to 18 mg/day.
 - Vanadium has never been shown to be effective for this purpose.

Carcinogenicity likely result of inhalation exposure

- ▶ Concern over potential carcinogenicity based on 2002 NTP inhalation study.
 - Incidence of lung neoplasms increased in male and female mice and in female rats – to a lesser degree.
 - No neoplasms were found in other organs.

Suggests observed effects were direct result of inhalation exposure route.

Reproductive toxicity likely secondary to general toxicity

- ▶ NIEHS notes that administration of tetravalent vanadium correlates with reductions in absolute epididymis weight and spermatid count.

“However, the results are not convincing, and significant general toxicity, reflected in decreased body weight gain, was also evident at 80 mg/kg body weight.”

International Programme on Chemical Safety, 2001.

NIEHS cites data from human volunteers

- ▶ 12 volunteers were given diammonium vanadotartrate at 75 mg/day for two weeks and then 125 mg/day for the next 5.5 months.
 - Reversible effects consisted of abdominal pain, nausea, and weight loss.
- ▶ 6 volunteers were given ammonium vanadyl tartrate at 50-125 mg/day for 45-90 days.
 - No toxic effects reported.
- ▶ Weight-training athletes were given vanadyl sulfate at 0.5 mg/kg/day for 12 weeks.
 - No toxic effects reported.

Summary and Recommendations

- ▶ Ingested vanadium is poorly absorbed and exhibits generally low toxicity.
- ▶ Typical oral exposures are below levels that might reasonably cause concern.
- ▶ Data from short-term and subchronic toxicity studies with human volunteers show no or reversible effects even at doses thousands of times greater than expected natural exposures.

We recommend that this nomination be assigned a low priority and that any proposed research rely on additional clinical and retrospective epidemiological studies.