EXECUTIVE SUMMARY

TEREPHTHALIC ACID (TPA) – Oral Risk Assessment CAS # 100-21-0

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>LEVEL</th>
<th>UNITS</th>
<th>DERIVED</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL (no-observed-adverse-effect level)</td>
<td>142</td>
<td>mg/kg-day</td>
<td>From a chronic dietary study in rats</td>
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<tr>
<td>Oral Rfd (oral reference dose)</td>
<td>0.5</td>
<td>mg/kg-day</td>
<td>From the NOAEL in rats with a 300x total uncertainty factor</td>
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<tr>
<td>TAC (total allowable concentration)</td>
<td>3</td>
<td>mg/L</td>
<td>For a 70 kg adult drinking 2 L/day using a 20% relative source contribution for drinking water</td>
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</tbody>
</table>

 EXPOSURE SUMMARY
Polyethylene terephthalate, a copolymer of terephthalic acid (TPA) or dimethyl terephthalate (DMT) with ethylene glycol, has food, beverage, and drinking water contact applications.

 KEY STUDY

 CRITICAL EFFECT
Bladder calculi and transitional cell adenoma were observed in the urinary bladder of female rats fed TPA for two years.

 UNCERTAINTY FACTORS
Factors applied in calculating the oral Rfd include:
- 10x for interspecies extrapolation
- 10x for intraspecies extrapolation
- 1x for subchronic to chronic extrapolation
- 1x for LOAEL to NOAEL
- 3x for database deficiencies
The total uncertainty factor is therefore 300x.

 TOXICITY SUMMARY
Bladder calculi and transitional cell adenoma were observed in the urinary bladder of female rats fed TPA for two years. The mode of action of TPA, and of dimethyl terephthalate (DMT), which is metabolized to TPA, involves urinary acidosis, altered electrolyte elimination and hypercalciuria, urinary supersaturation with calcium terephthalate or calcium hydrogen terephthalate, and crystallization into bladder calculi. Weanling rats were more sensitive to calculus formation than dams. Calculi-induced irritation led to bladder hyperplasia and tumors in rats fed 1000 mg/kg-day TPA. The lack of effects at 142 mg/kg-day supports a threshold for urine saturation with calcium terephthalate, a key event for calculus formation. There is no evidence to suggest that exposure to TPA, DMT, or the structurally-related terephthalates represent a genotoxic risk. Based on U.S. EPA (2005) cancer risk assessment guidelines, TPA requires two weight-of-evidence descriptors. At doses relevant to human exposure, there is inadequate information to assess the carcinogenic potential of TPA, because there are no human data and chronic testing has been performed in only one species. At very high doses of >2,000 mg/day at which urinary tract calculi may form, there is suggestive evidence of carcinogenic potential due to the non-genotoxic, but proliferative irritation effect of bladder calculi.

 CONCLUSIONS
The oral Rfd of 0.5 mg/kg-day for TPA and corresponding TAC in drinking water of 3 mg/L is protective of human health including sensitive populations.