**S1 Table.** **Schematic overview for placement of individual human and animal studies in study quality categories (1 st tier, 2nd tier, 3rd tier).** Adapted from the approach recommended by the National Toxicology Program's Office of Health Assessment and Translation (2015)1. “++” definitely low risk of bias, “+” probably low risk of bias, “-“ probably high risk of bias, “--“ definitely high risk of bias

|  |  |  |
| --- | --- | --- |
|  | **Key criteria** | **Other criteria** |
| **Category** | **Guidance** |  |  | **Identical experimental conditions** | **Confidence exposure characterization** | **Confidence outcome assessment** | Randomization exposure level | Allocation concealment | Blinding | Attrition/Exclusion rate | Reporting | Other potential threats |
| 1st tier | “definitely low” or “probably low” risk of bias for all key criteriaAND“definitely low” or “probably low” risk of bias for more than half of the other applicable criteria |  |  |  |  |  |  |  |  |  |  |  |
| Example 1 | ++ | ++ | + | + | - | - | ++ | + | + |
|  |  |  |  |  |  |  |  |  |  |  |
| 2nd tier | study does not meet criteria for tier 1 or tier 3 | Example 2 | ++ | - | ++ | + | - | - | + | ++ | - |
| Example 3 | + | - | - | - | - | ++ | -- | + | + |
| Example 4 | - | - | - | + | + | - | + | - | + |
| 3rd tier | “probably high” or “definitely high” risk of bias for all key criteriaAND“definitely high” or “probably high” risk of bias for more than half of the other applicable criteria |  |  |  |  |  |  |  |  |  |  |  |
| Example 5 | -- | - | - | - | + | - | + | - | - |
|  |  |  |  |  |  |  |  |  |  |  |

**1** National Toxicology Program (NTP), 2015a. Handbook for conducting a literature-based health assessment using OHAT approach for systematic review and evidence integration. Office of Health Assessment and Translation. <http://ntp.niehs.nih.gov/go/38673>.