Supplemental Table 1. Risk of bias questions and evidence needed for a “Definitely Low Risk of Bias” rating. A “Probably Low Risk of Bias” generally relied on similar criteria but indirect evidence or the component would not appreciably bias results.

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| Question | Direct Evidence That: |
| Was administered dose or exposure level adequately randomized? | Animals were allocated to control and treatment groups using a random method (e.g., referring to a random number table, using a computer random number generator, coin tossing, shuffling cards, blocked randomization, or stratified randomization [e.g., body weight]). |
| Was allocation to study groups adequately concealed? | Research personnel did not know how animals were allocated and allocation remained unknown until after assignment was completed |
| Were experimental conditions identical across study groups? | Same vehicle was used in control and experimental animals, and non-treatment-related experimental conditions were identical across study groups |
| Were research personnel blinded to the study group during the study? | Research personnel were adequately blinded to study group (e.g., central allocation; sequentially numbered treatment containers of identical appearance; sequentially numbered animal cages; or equivalent methods). |
| Were outcome data complete without attrition or exclusion from analysis? | Loss of animals was adequately addressed and reasons were documented when animals were removed from a study, Or missing data have been imputed using appropriate methods. |
| Can we be confident in the exposure characterization? | Exposure to the PBDE was independently characterized and confirmed generally as ≥98% purity (including mixtures) and exposure was consistently administered across treatment groups, and for gavage, dietary, or drinking water studies, that information is provided on consumption or internal dose metrics to confirm expected exposure levels sufficiently to allow discrimination between exposure groups, and if internal dose metrics are available, there is evidence that most of the exposure data measurements are above the limit of quantitation for the assay such that different exposure groups can be distinguished. |
| Can we be confident in the outcome assessment? | The outcome was assessed using well-established methods (e.g., Morris water maze, radial arm maze, operant tests of cognition), and assessed at the same length of time (i.e., same day of life) after initial exposure in all study groups, and the outcome assessors were adequately blinded to the study group, and it is unlikely that they could have broken the blinding prior to reporting outcomes. |
| Were all measured outcomes reported? | All of the study’s measured outcomes outlined in the protocol, methods, abstract, and/or introduction (that are relevant for the evaluation) have been reported. |
| Control for litter effects | Litter effects were appropriately considered in the study design or analysis, using one of the following approaches: the dam was used as the statistical unit of analysis, or the fetus/pup used as the statistical unit of analysis and litter effects were appropriately considered in the analysis and the statistical method was stated. |

Supplemental Table 2. PBDE studies used in the meta-analysis of latency in the last acquisition trial of the Morris Water Maze.

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| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  | Morris Water Maze Methods | | | |
| Study | Chemical | Doses (mg/kg-day) | Species/strain/life stage assessed | Number of sessions per day | Initial entry location | Session length (sec) | Number of consecutive days |
| Chen et al. 2014 | BDE-209 | 0, 10.0, 30, 50 | Rat/Sprague-Dawley/PND 25 | 4 | Rats entered the maze from a different point on each day. | 60 | 4 |
| Cheng et al. 2009 | BDE-99 | 0, 2 | Rat/Sprague-Dawley/PND 34-36 | 4 | Each quadrant was used once on each day. | 120 | 3 |
| He et al. 2011 | BDE-47 | 0, 1, 5, 10 | Rat/Sprague-Dawley/2 months | 4 | Initial entry location was not specified. | 60 | 3 |
| Verma et al. 2013 | BDE-209 | 0, 20 | Mouse/Swiss albino/PND 60-66 | 4 | Single target quadrant used. Initial entry location was not specified. | 120 | 6 |
| Viberg et al. 2003 | BDE-153 | 0, 0.45, 0.9, 9 | Mouse/NMRI/PND 180 | 5 | Single entry quadrant used. | 30 | 4 |
| Woods et al. 2012 | BDE-47 | 0, 0.03 | Mouse/Mecp2 308+/- or wild type/PND 50-54 | 4 | Initial entry location was not specified. | 90 | 4 |

Supplemental Table 3. Overall analyses and sensitivity analyses of studies of PBDEs and latency in the last trial of the Morris Water Maze. Reprinted with permission (NASEM, 2017).

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Analysis | Estimate | Beta | CI, Lower Bound | CI, Upper Bound | P value | tau | I2 | P value for Heterogeneity | AICc |
| *Primary Analyses* | | | | | | | | | |
| Overall | intrcpt | 25.76 | 20.32 | 31.19 | 0.000000 | 4.65 | 24.46 | 0.2685 | 101.48 |
| Trend in log10(dose) | log10(dose) | 5.74 | -2.16 | 13.63 | 0.154334 | 3.41 | 14.58 | 0.3825 | 96.49\* |
| Linear in dose10 | dose10 | 9.61 | 3.79 | 15.42 | 0.001209 | 17.12 | 81.59 | 0.0000 | 116.50 |
| Linear-Quadratic in dose10 | dose10  I(dose10^2) | 28.07 | 11.22 | 44.91 | 0.001093 | 13.92 | 72.33 | 0.0001 | 108.36 |
| -4.45 | -8.30 | -0.60 | 0.023373 | 13.92 | 72.33 | 0.0001 | 108.36 |
| *Sensitivity Analyses* | | | | | | | | | |
| Overall minus Viberg et al. 2003 | intrcpt | 25.77 | 20.07 | 31.46 | 0.000000 | 4.95 | 32.02 | 0.1180 | 77.61 |
| Overall minus Chen et al. 2014 | intrcpt | 25.60 | 18.33 | 32.86 | 0.000000 | 5.17 | 22.40 | 0.3185 | 81.54 |
| Overall minus Verma et al. 2013 | intrcpt | 25.52 | 20.08 | 30.97 | 0.000000 | 4.65 | 26.04 | 0.3070 | 90.62 |
| Overall minus He et al. 2011 | intrcpt | 27.13 | 20.03 | 34.22 | 0.000000 | 4.14 | 13.54 | 0.4338 | 81.26 |
| Overall minus Woods et al. 2012 | intrcpt | 25.87 | 20.38 | 31.36 | 0.000000 | 4.64 | 27.53 | 0.2743 | 82.77 |
| Overall minus Cheng et al. 2009 | intrcpt | 25.12 | 19.24 | 30.99 | 0.000000 | 5.03 | 27.26 | 0.2377 | 94.83 |
| Highest Doses-Overall | intrcpt | 32.95 | 26.67 | 39.23 | 0.000000 | 0.00 | 0.00 | 0.6596 | 56.49 |
| Highest Doses-Overall minus Viberg et al. 2003 | intrcpt | 32.91 | 26.55 | 39.26 | 0.000000 | 0.00 | 0.00 | 0.5325 | 50.67 |
| Highest Doses-Overall minus Chen et al. 2014 | intrcpt | 32.39 | 24.92 | 39.86 | 0.000000 | 0.00 | 0.00 | 0.5419 | 52.83 |
| Highest Doses-Overall minus Verma et al. 2013 | intrcpt | 32.67 | 26.38 | 38.97 | 0.000000 | 0.00 | 0.00 | 0.7322 | 47.94 |
| Highest Doses-Overall minus He et al. 2011 | intrcpt | 33.34 | 24.55 | 42.14 | 0.000000 | 0.00 | 0.00 | 0.5336 | 53.08 |
| Highest Doses-Overall minus Woods et al. 2012 | intrcpt | 33.32 | 26.95 | 39.70 | 0.000000 | 0.00 | 0.00 | 0.8448 | 45.18 |
| Highest Doses-Overall minus Cheng et al. 2009 | intrcpt | 33.13 | 26.28 | 39.98 | 0.000000 | 0.00 | 0.00 | 0.5337 | 52.46 |
| Highest Doses-Trend in log10(dose) | log10(dose) | 3.40 | -6.47 | 13.28 | 0.499553 | 0.00 | 0.00 | 0.5978 | 70.61 |
| Highest Doses-Linear in dose10 | dose10 | 10.01 | 0.06 | 19.95 | 0.048547 | 26.04 | 88.45 | 0.0000 | 67.93 |
| Highest Doses-Linear-Quadratic in dose10 | dose10 | 48.56 | 17.03 | 80.08 | 0.002536 | 15.99 | 55.56 | 0.0236 | 76.79 |
| I(dose10^2) | -8.34 | -14.87 | -1.81 | 0.012356 |  |  |  |  |  |

\* Indicates the lowest AICc.