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## Supplemental Material

# Beyond the RfD: Broad Application of a Probabilistic Approach to Improve Chemical Dose–Response Assessments for Noncancer Effects

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**Figure S1. Comparison across sources for Reference Doses (A), Points of Departure (B), and Endpoint-specific Reference Doses (C) for the same chemical evaluated.** No comparisons were performed for PPRTVs and HEAST because these sources had very few, if any, (between 0 and 3) overlapping chemicals with other sources. ATSDR = Agency for Toxic Substances and Disease Registry; HEAST = Health Effects Assessment Summary Tables; IRIS = U.S. EPA Integrated Risk Information System; OPP = U.S. EPA Office of Pesticide Programs; PPRTV = Provisional Peer-Reviewed Toxicity Values.

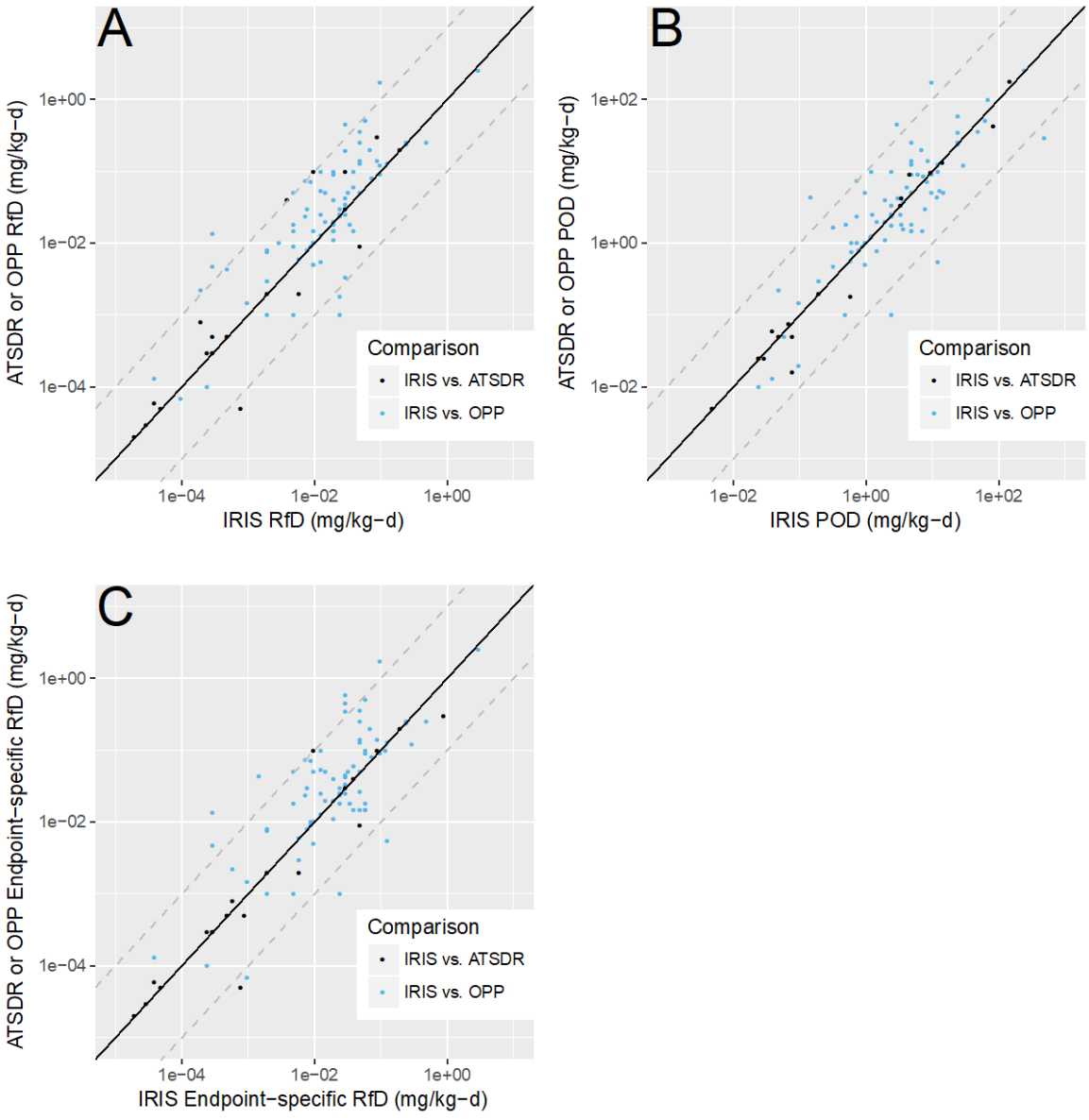
**Figure S2. Comparison of "Approximate" Calculation Results with Monte-Carlo Simulation-Based Estimates.** The boxplots present the ratio between the "approximate" calculations and Monte Carlo-based results using 10 million samples, for the lower 95% confidence (P05), median (P50), and upper 95% confidence (P95) estimates of the $HD_M^I$. Each boxplot includes the interquartile range (box), median (line in box), 95% confidence interval (whiskers), and values outside 95% confidence interval (circles).

**Figure S3. Comparison of results of traditional and probabilistic dose-response assessment, separated by endpoint.** Scatterplot of traditional RfD versus probabilistic RfD, defined as shown in **Figure 1** for I=1%. Solid line denotes equality, and black circles are traditional and probabilistic RfDs, with each panel a subset based on endpoint, as labeled.

**Figure S4. Comparison of results of traditional and probabilistic dose-response assessment, separated by Point of Departure (POD).** Scatterplot of traditional RfD versus probabilistic RfD, defined as shown in **Figure 1** for I=1%. Solid line denotes equality, and black circles are traditional and probabilistic RfDs, with each panel a subset based on POD, as labeled. BMDL = benchmark dose lower confidence limit; NOAEL = No Observed Adverse Effect Level; LOAEL = Lowest Observed Adverse Effect Level.

**Figure S5. Comparison of results of traditional and probabilistic dose-response assessment, separated by decade of assessment.** Scatterplot of traditional RfD versus probabilistic RfD, defined as shown in **Figure 1** for I=1%. Solid line denotes equality, and black circles are traditional and probabilistic RfDs, with each panel a subset based on the decade in which the traditional RfD was published, as labeled.

## Supplemental Figures

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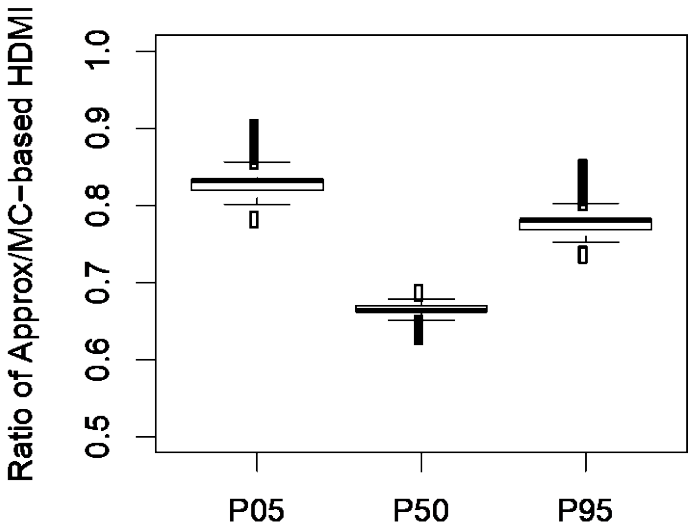


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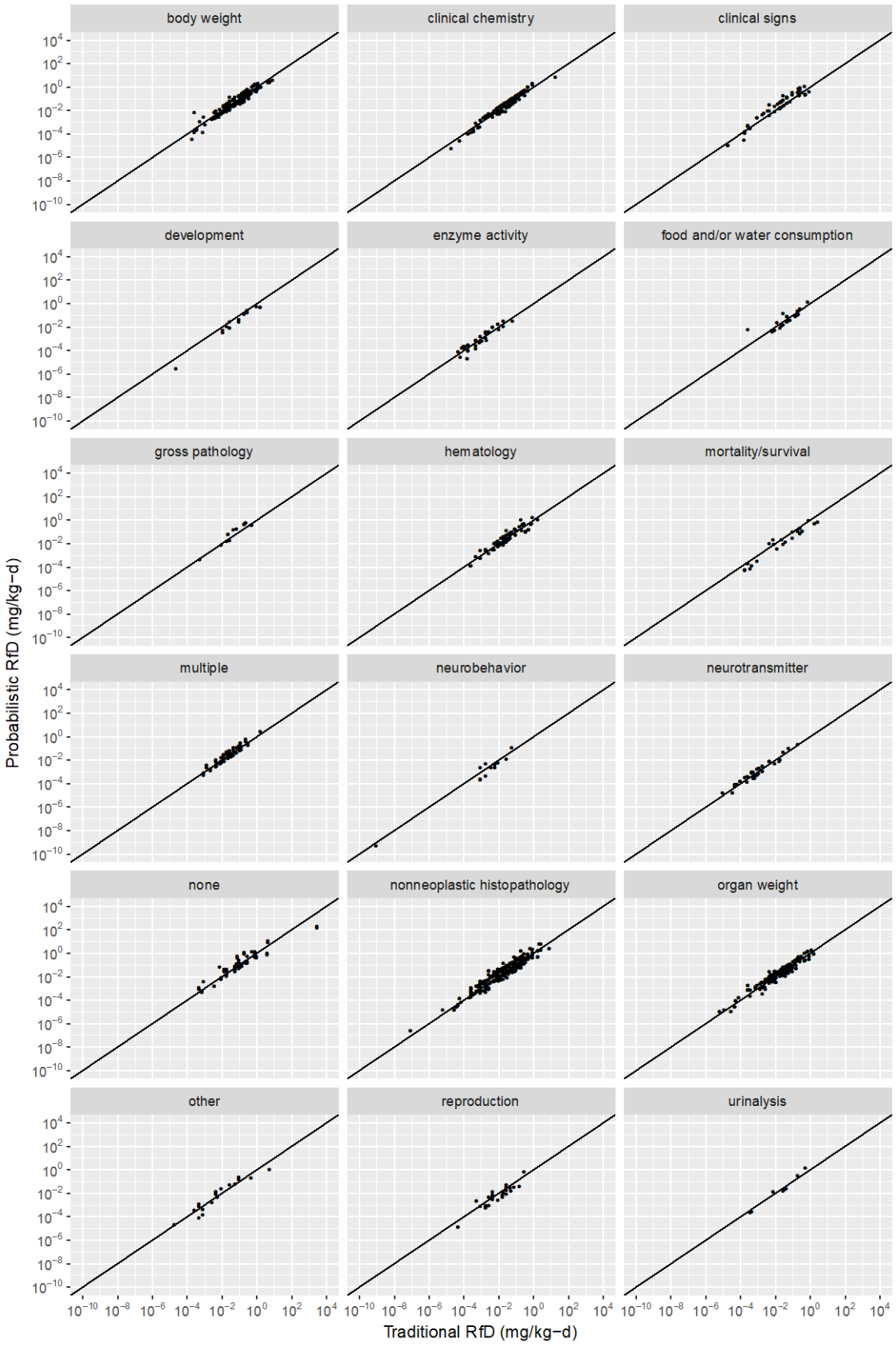
body weight
clinical chemistry
clinical signs
development
enzyme activity
food and/or water consumption
gross pathology
hematology
mortality/survival
multiple
neurobehavior
neurotransmitter
none
nonneoplastic histopathology
organ weight
other
reproduction
urinalysis
Probabilistic RfD (mg/kg−d)
Traditional RfD (mg/kg−d)
$10^{-10}$ $10^{-8}$ $10^{-6}$ $10^{-4}$ $10^{-2}$ $10^{0}$ $10^{2}$ $10^{4}$

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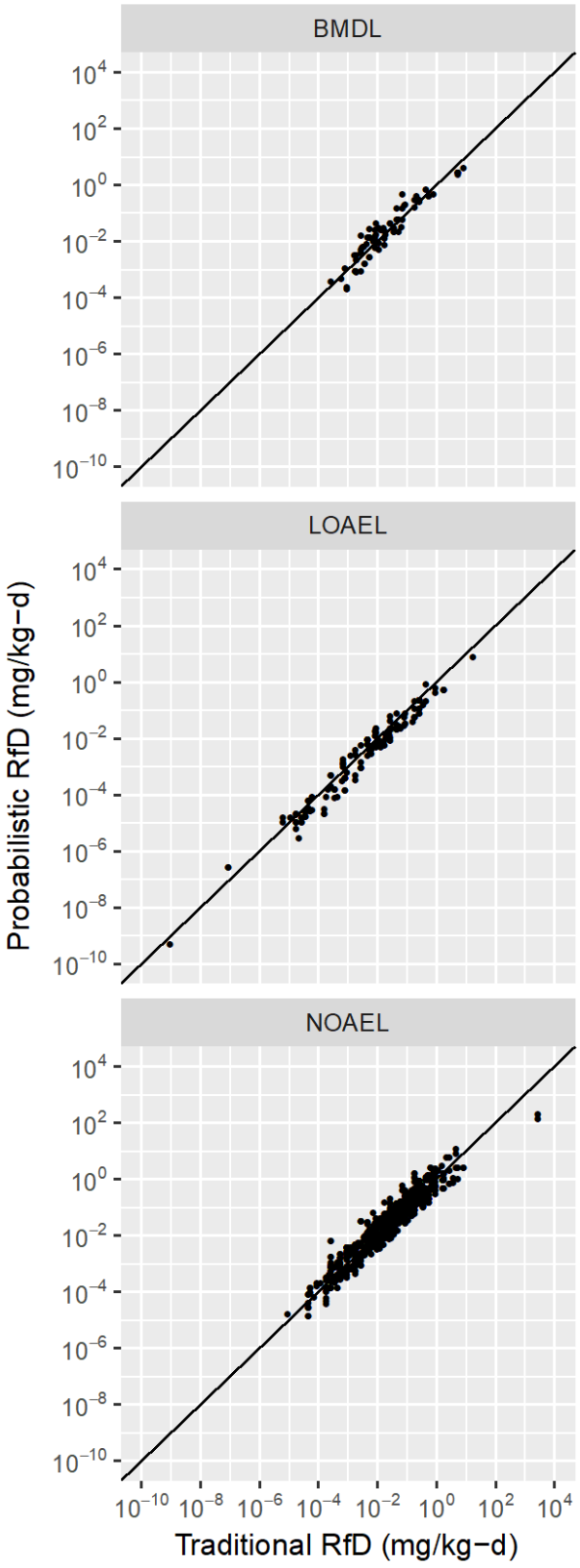
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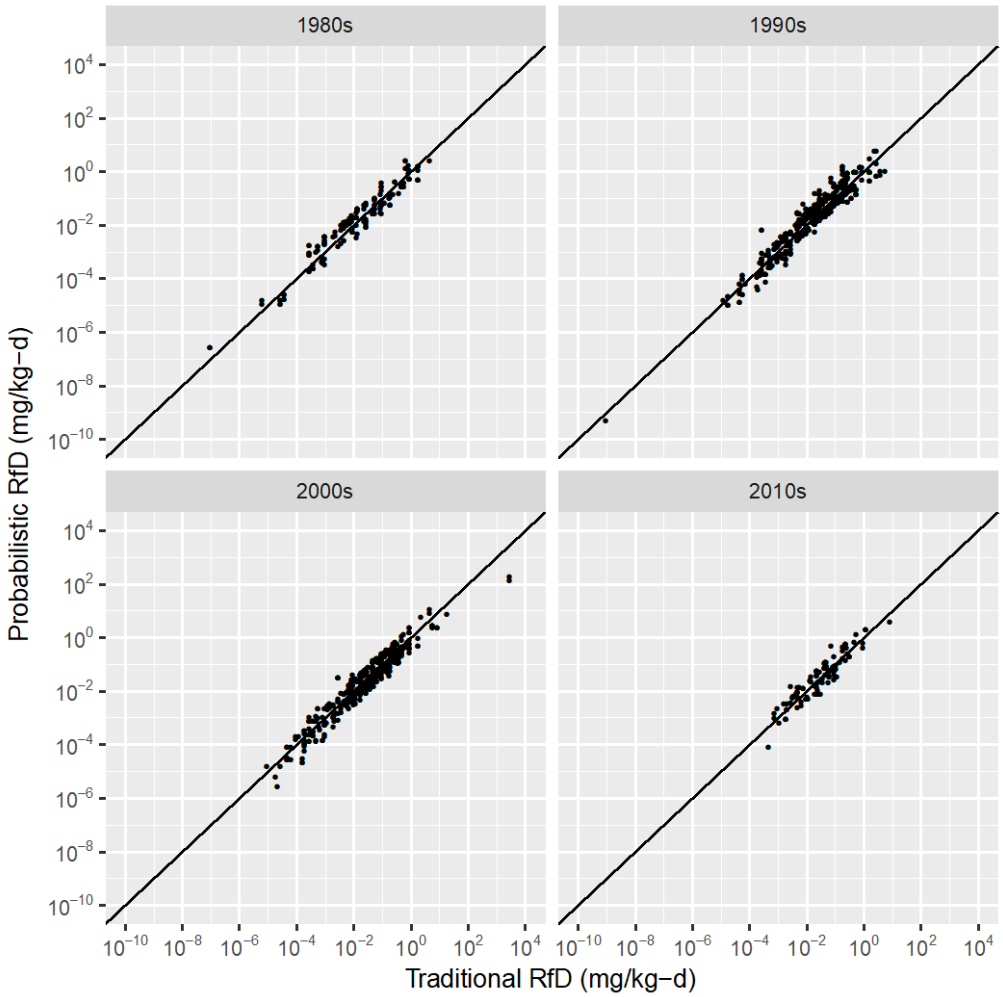


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