

## SUPPLEMENTARY MATERIALS

**Supplementary Table 1.** Cancer outcomes and contributing ICD-10 codes.

| Cancer site or type   | ICD-10 code(s)   |
|-----------------------|--|
| Leukemia              | C91.0, C91.1, C91.6, C91.7, C91.9, C92.0, C92.1, C92.4, C92.5, C92.7, C92.9, C93.0, C93.1, C93.3, C93.7, C94.0, C94.2, C94.6, C94.7, C95.0, C95.7, C95.9   |
| Lymphoma              | C81.0, C81.1, C81.2, C81.4, C81.7, C81.9, C82.9, C83.3, C83.5, C83.6, C83.7, C83.9, C84.0, C84.5, C84.6, C85.1, C85.7, C85.9, C96.0, C96.1, C96.3, C96.5, C96.6, C96.9   |
| Brain/CNS             | C70.0, C70.9, C71.0, C71.1, C71.2, C71.3, C71.4, C71.5, C71.6, C71.7, C71.8, C71.9, C72.0, C72.3, C72.8, C72.9, C75.2, C75.3, C75.5  |
| Neuroblastoma         | C47.0, C47.1, C47.4, C47.6, C47.8, C47.9, C74.0, C74.1, C74.9  |
| Retinoblastoma        | C69.2, C69.3, C69.4, C69.6, C69.8, C69.9   |
| Kidney                | C64.9  |
| Liver                 | C22.0, C22.2, C22.7, C22.9   |
| Osteosarcoma          | C30.0, C30.1, C31.0, C31.9, C40.0, C40.1, C40.2, C40.3, C40.9, C41.0, C41.1, C41.2, C41.3, C41.4, C41.9  |
| Soft tissue sarcoma   | C49.0, C49.1, C49.2, C49.3, C49.4, C49.5, C49.6, C49.8, C49.9, C51.9, C52.9, C53.9, C63.2, C67.9, C76.0, C76.1, C76.2, C76.3, C76.4, C76.5, C76.7  |
| Reproductive organ    | C56.9, C57.9, C62.1, C62.9, C80.9  |
| Other or unclassified | C00.9, C02.1, C02.2, C03.1, C04.9, C05.1, C06.9, C07.9, C08.9, C09.0, C09.9, C10.9, C11.0, C11.9, C13.9, C18.1, C18.2, C18.4, C34.9, C43.0, C43.1, C43.2, C43.3, C43.4, C43.5, C43.6, C43.7, C43.9, C44.0, C44.3, C44.4, C44.5, C44.5, C44.5, C44.6, C44.7, C44.7, C44.9, C48.0, C48.2, C48.8, C73.9, C76.0, C76.0, C76.1, C76.2, C76.3, C76.4, C76.5, C20.9, C25.0, C25.8, C38.1, C38.3, C45.1, C46.7, C65.9, C77.0, C77.3, C77.4, C77.9, C78.0, C78.8, C79.2, C79.3, C86.6, C88.3, C88.4 |

**Supplementary Table 2.** Summary of phthalate-containing medications prescribed to the cohort.<sup>a</sup>

| Medication        | ATC code | CAP | DBP | DEP | HPMCP | PVAP | Phthalate-free |
|-------------------|----------|-----|-----|-----|-------|------|----------------|
| Bisacodyl         | A06AB02  |     | 9   | 7   | 5     | —    | 14             |
| Budesonide        | A07EA06  | —   | 2   | —   | —     | —    | 40             |
| Clarithromycin    | J01FA09  | —   | —   | —   | 9     | —    | 71             |
| Combinations      | B01AC30  | —   | —   | —   | 2     | —    | 11             |
| Diclofenac        | M01AB05  | 2   | 3   | 2   | —     | —    | 214            |
| Diclofenac combi  | M01AB55  | 2   | —   | 2   | —     | —    | 23             |
| Dipyridamole      | B01AC07  | —   | —   | —   | 3     | —    | 21             |
| Duloxetine        | N06AX21  | —   | —   | —   | 11    | —    | 52             |
| Erythromycin      | J01FA01  | —   | —   | 16  | 16    | —    | 44             |
| Esomeprazole      | A02BC05  | —   | —   | 5   | —     | —    | 185            |
| Fluoxetine        | N06AB03  | —   | —   | 2   | —     | —    | 79             |
| Ibuprofen         | M01AE01  | —   | —   | 13  | —     | —    | 163            |
| Lithium           | N05AN01  | —   | 2   | —   | —     | —    | 2              |
| Mesalazine        | A07EC02  | —   | 6   | —   | —     | —    | 101            |
| Mianserin         | N06AX03  | —   | —   | 14  | —     | —    | 50             |
| Multienzymes      | A09AA02  | 2   | 4   | 2   | 15    | —    | 64             |
| Mycophenolic acid | L04AA06  | —   | —   | —   | 2     | —    | 17             |
| Naproxen          | M01AE02  | 28  | —   | 8   | —     | —    | 88             |
| Pentoxyverine     | R05DB05  | 2   | —   | —   | —     | —    | 2              |

|               |         |    |   |    |   |   |    |
|---------------|---------|----|---|----|---|---|----|
| Propantheline | A03AB05 | 3  | — | —  | — | — | 3  |
| Rabeprazole   | A02BC04 | —  | — | —  | 7 | — | 9  |
| Sulfasalazine | A07EC01 | 3  | — | —  | — | — | 35 |
| Theophylline  | R03DA04 | 13 | — | 8  | — | — | 20 |
| Valproic acid | N03AG01 | 21 | — | —  | — | 9 | 85 |
| Verapamil     | C08DA01 | —  | — | 13 | — | — | 85 |

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<sup>a</sup>Cell frequencies are the number of unique drug products in each phthalate content category. Note that some phthalate-containing drug products were formulated with more than one type of phthalate. ATC: Anatomical therapeutic chemical classification system; CAP: Cellulose acetate phthalate; DBP: Dibutyl phthalate; DEP: Diethyl phthalate; HPMCP: Hydroxypropyl methylcellulose phthalate; PVAP: Polyvinyl acetate phthalate.

**Supplementary Table 3.** Associations between childhood phthalate exposure and type-specific cancer incidence, before and after semi-Bayes adjustment.<sup>a</sup>

| Cancer type                  | Analysis   | HR (95% CI)       |
|------------------------------|------------|-------------------|
| Leukemia - combined          | Semi-Bayes | 0.96 (0.64, 1.43) |
|                              | Original   | 0.85 (0.55, 1.30) |
| Leukemia - acute lymphocytic | Semi-Bayes | 0.95 (0.61, 1.47) |
|                              | Original   | 0.81 (0.50, 1.32) |
| Leukemia - acute myeloid     | Semi-Bayes | 1.28 (0.72, 2.28) |
|                              | Original   | 1.22 (0.44, 3.37) |
| Lymphoma - combined          | Semi-Bayes | 1.87 (1.28, 2.75) |
|                              | Original   | 2.07 (1.36, 3.14) |
| Lymphoma - non-Hodgkin       | Semi-Bayes | 1.86 (1.14, 3.02) |
|                              | Original   | 2.29 (1.33, 3.92) |
| Lymphoma - Hodgkin           | Semi-Bayes | 1.62 (0.96, 2.73) |
|                              | Original   | 2.04 (1.01, 4.12) |
| Lymphoma - Burkitt           | Semi-Bayes | 1.27 (0.65, 2.46) |
|                              | Original   | 0.90 (0.12, 6.75) |
| Brain/CNS                    | Semi-Bayes | 1.05 (0.62, 1.78) |
|                              | Original   | 0.84 (0.43, 1.65) |
| Neuroblastoma                | Semi-Bayes | 1.39 (0.76, 2.53) |
|                              | Original   | 1.57 (0.49, 5.04) |
| Retinoblastoma               | Semi-Bayes | (Not estimable)   |
|                              | Original   | (Not estimable)   |
| Kidney                       | Semi-Bayes | 1.29 (0.71, 2.34) |
|                              | Original   | 1.17 (0.37, 3.72) |
| Liver                        | Semi-Bayes | 1.31 (0.68, 2.52) |
|                              | Original   | 1.18 (0.16, 8.86) |
| Osteosarcoma                 | Semi-Bayes | 2.10 (1.24, 3.55) |
|                              | Original   | 2.78 (1.63, 4.75) |
| Soft tissue sarcoma          | Semi-Bayes | 1.20 (0.67, 2.15) |
|                              | Original   | 0.98 (0.36, 2.69) |
| Reproductive organ           | Semi-Bayes | 1.16 (0.56, 2.40) |
|                              | Original   | 0.38 (0.05, 2.78) |

|       |            |                   |
|-------|------------|-------------------|
| Other | Semi-Bayes | 1.10 (0.68, 1.78) |
|       | Original   | 0.95 (0.52, 1.75) |

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<sup>a</sup>HR = hazard ratio; CI = confidence interval; CNS = central nervous system

**Supplementary Figure 1.** Comparison of associations between childhood phthalate exposure and type-specific cancer incidence under original and alternative exposure definitions. In the original analysis, exposure was defined as receiving at least one prescription fill with a phthalate-containing drug product. In the sensitivity analysis, exposure was defined as receiving at least two prescription fills with a phthalate-containing drug product. Subjects were classified as unexposed until meeting the respective exposure definition. Comparison is limited to the 13 type-specific cancers with estimable associations in both analyses. Error bars represent the 95% confidence intervals (CIs). CNS=central nervous system.

